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# NOCARDIOSIS CUTIS RESEMBLING SPOROTRICHOSIS

## REPORT OF A CASE

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Since 1898, when Schenk [1] reported his studies on refractory subcutaneous abscesses caused by a fungus possibly related to the sporotricha, over 200 proved cases and innumerable probable cases of sporotrichosis have been reported. Beurman and his associates made the bulk of these observations and while the clinical picture was different from that described by American authors and certain differences from the original fungus were noted, it is considered that these observations serve only to establish the identity of several subtypes of the same infection. Cases of sporotrichosis have been reported in this country by Hektoen and Perkins,[2] Hyde and Davis,[3] Hamburger,[4] Sutton,[5] Lewis,[6] Pusey,[7] Stelwagon,[8] Olson,[9] Blaisdell,[10]

1. Schenk, B. R.: On Refractory Subcutaneous Abscesses Caused by a Fungus Possibly Related to the Sporotricha, Bull. Johns Hopkins Hosp., December, 1898, p. 286.

2. Hektoen, L., and Perkins, C. F.: Refractory Subcutaneous Abscesses Caused by Sporothrix Schenckii, a New Pathogenic Fungus, J. Exper. Med. **5**:77 1900.

3. Hyde, J. N., and Davis, D. J.: Sporotrichosis in man, with Incidental Consideration of Its Relation to Mycotic Lymphangitis in Horses, J. Cutan. Dis. **28**:32 (July) 1910.

4. Hamburger, Walter W.: Sporotrichosis in Man, J. A. M. A. **59**:1590 (Nov. 2) 1912.

5. Sutton, Richard L.: Sporotrichosis in America, J. A. M. A. **55**:2213 (Dec. 24) 1910.

6. Lewis, Dean: Blastomycosis and Sporotrichosis, Surg. Clin. Chicago **1**:1125 (Dec.) 1917.

7. Pusey, W. A.: The Therapeutic Use of Refrigeration, Particularly with Solid Carbon Dioxid, J. Cutan. Dis. **28**:352, 1910.

8. Stelwagon, H. W.: Short discussion of the Hyde and Davis Paper, J. Cutan Dis. **28**:144, 1910.

9. Olson, G. M.: A Case of Sporotrichosis in North Dakota. Probable Infection from Gophers, J. A. M. A. **59**:941 (Sept. 21) 1912.

10. Blaisdell, J. H.: A Clinical and Histopathological Report of the First Case to Be Published in New England, J. Cutan. Dis. **35**:452 (Aug.) 1917.

Moore,[11] Laine [12] and others and the clinical picture in practically every instance has been that of the sporotrichotic chancre with an ascending lymphangitis. In most of these cases, the sporotrichium of Schenck was demonstrated. Therefore, a case that agrees with the description of sporotrichosis clinically, but found to be caused by an organism other than the sporotrichium of Schenck, is considered worthy of a special report.

## REPORT OF CASE

*History.*—In July, 1919, C. L., a man, single, aged about 50 years, a coal miner, was referred for diagnosis and treatment. He was suffering from a number of inflammatory lesions extending in linear fashion from the base of the left thumb to a point slightly above the bend of the elbow.

The following rather incomplete history was obtained. About six months before presenting himself, there appeared at the base of the left thumb "a small pimple" to which no attention was paid. In about two weeks the lesion developed to about the size of a pea and a drop of pus formed in it. This was pricked with a pin and various home remedies applied without materially affecting the lesion, which developed into an indolent ulceration one-half inch in diameter. About this time a second "pimple" appeared close

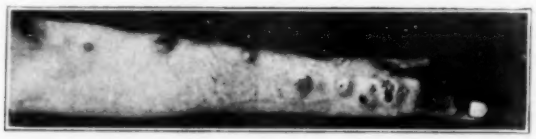

Fig. 1.—Nocardiosis of the hand and arm of author's patient.

to the proximal side of the first one. This lesion was treated in the same manner as the original focus with the same result. In about a month a third lesion appeared close to the second. This one developed into a larger lesion than either of the two earlier ones, and finally discharged a considerable amount of thick pus. Others appeared at intervals until a complete chain of lesions in various stages of development extended from the site of the chancre to the latest lesion which had appeared as a "little pimple or lump" within the preceding seven days. At no time had the patient's general health been affected, and the lesions themselves gave little discomfort.

*Appearance of the Condition When First Seen.*—The site of the early lesions was occupied by a superficial indurated ulceration, irregular in outline, evidently formed by confluence of two or more smaller ulcers. The edges were ragged and the base was covered with an indolent appearing granulating tissue. Extending from this point to just above the bend of the elbow was a chain of hazelnut sized inflammatory nodules with soft centers, the two nearest the ulcer being of a doughy consistence. Those nearest the bend of the elbow were firm and were graded in size from the largest of the lesions

11. Moore: Reporting a Case at the Meeting of the Chicago Dermatological Society, J. Cutan. Dis. **35**:609, 1917.

12. Lain, E. S.: Sporotrichosis, State M. J. Oklahoma M. A. **13**:41 (Feb.) 1920.

to the week-old lesion, which was about the size of a split pea, firm to the touch, moderately inflammatory and firmly fixed in the skin. None of the lesions were as tender as they appeared to be.

*Bacteriology.*—Under aseptic precautions, one of the large soft unbroken lesions was opened and various culture mediums inoculated. After forty-eight hours, at room temperature, there appeared on agar several grayish white pinhead sized colonies, rather dense at the center, with a fine radiating fringe. This was found to be made up of a mass of tangled branching threads, bearing small granules. Older cultures showed the presence of these fine granules between the threads.

*Histopathology.*—The youngest lesion which, according to the patient, was about a week old, was removed and paraffin sections made at the W. H.

Fig. 2.—Arrangement of the threads and the infiltration.

Singer Memorial Laboratory under the supervision of Drs. S. R. Haythorn and G. R. Lacy, to whom I am also indebted for the original bacteriologic work. No changes of moment were noted in the epidermis. In the derma there was a more or less circumscribed infiltration rather thin superficially and becoming more dense at about the level of the coil glands. The tissues generally were intensely edematous and in places the collagenous tissues showed a tendency toward basic staining. The blood vessels were more or less dilated and in places surrounded by a moderate cellular infiltration. The focus of the infection was deep in the derma, in and about markedly dilated lymphatic spaces and vessels. The infiltration was largely lymphocytic or round cell in type, there being, however, a goodly number of epithelioid cells and a few polymorphonuclear leukocytes. One ill-formed giant cell was noted. By the Gram-

Weigert method of staining, numbers of parallel and tangled threads were demonstrated in and about dilated lymphatic vessels and spaces at the focus of infection mentioned above.

*Classification of the Organism.*—Dr. W. L. Holman of the department of bacteriology at the University of Pittsburgh has supplied the following notes:

"The micro-organism grown from and seen in the tissues of this case should be classified under the Actinomycetaceae.[13] The Actinomycetaceae is divided

Fig. 3.—Low power drawing showing location of the focus.

into two species—Actinomyces, including the anaerobic species, and Nocardia, including the common saprophytic soil forms, as well as a number of pathogenic species.

"The further classification of the Nocardial strain here reported is practically impossible in the present state of our knowledge and the confusion of

13. Breed and Conn: Nomenclature of the Actinomycetaceae, J. Bacteriol. **4**:585, 1919. Foulerton: Nature of Parasites of Leprosy and Tuberculosis (a Discussion of Streptothrix and Allied Forms), Brit. M. J. **2**:300, 1912.

nomenclature. The morphologic picture of tangled, branching threads, with granules or 'spores' in the threads or, in older cultures, free in the medium, the nodular appearance and the manner of growth on and in mediums, all indicated that it is closely allied to the air Nocardia. The presence of thread formation in the tissues, without spore forms, precludes it being grouped with the Sporothrix, Coccidioides or Blastomyces. Further, it differs radically from all of these in microscopic morphology from cultures and the type of colony developed on mediums.

"The Sporothrix is a closely allied but higher fungus with branching, septate mycelium which forms yeast-like 'spore' bodies, within and budding from the mycelium. In the tissues it shows, almost exclusively, these elongated yeast forms. The so-called spores of Nocardia resemble short rods or coccoid

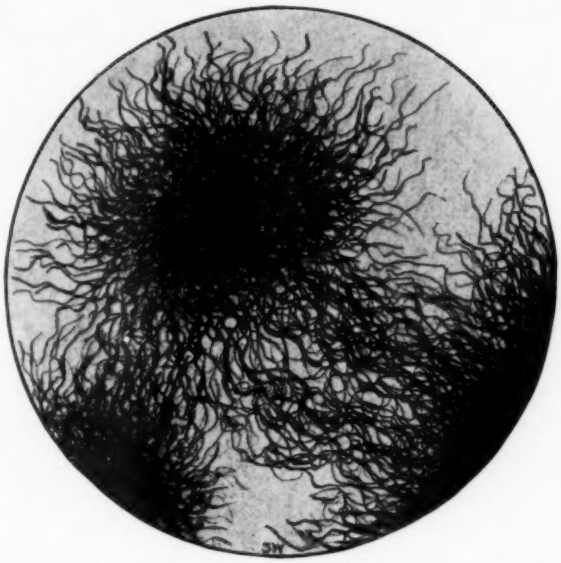

Fig. 4.—A four day old hanging drop culture.

forms of the organism and are much smaller than the yeast-like 'spores' of Sporothrix. Streptothrix has been dropped from the nomenclature of these thread forms."

*Further Notes on the Case.*—When first seen, a clinical diagnosis of sporotrichosis was made, and the patient was supplied with a saturated solution of the iodid of potassium. He was instructed to take ten drops in water three times a day, increasing the dose one drop a day. Nothing else was done except to apply simple protective dressings, and the patient made an uninterrupted recovery.

## HISTORICAL

Under the term nocardia is included a considerable number of more or less closely related organisms, the pathogenicity of which have been demonstrated in several different clinical conditions, although there are also many nonpathogenic members of the family. The name is applied to the group on grounds of priority because

Nocard first described such an organism, which he isolated from the superficial abscesses of cattle suffering from farcy.

For a concise summary of the subject of nocardiosis, the reader is referred to an article by J. H. Wright.[14] The process in most of the cases at that time had been in the lung or had originated there. Signs of empyema were present in two cases, in one of which there was an inflammatory fluctuating tumor on the external aspect of the chest wall. In two cases there were multiple metastatic abscesses in the subcutaneous tissues with symptoms of pyemia. In one of these, infection with the bacillus of glanders was suspected. In a few cases the process has been essentially of the character of a terminal infection. In three of the cases there was abscess formation in the brain. In the case of subacute peritonitis with gastrotomy, the prominent symptom was diarrhea.

In 1913, Potron and Thiry [15] reported a case of nocardiosis involving the skin of the neck with small vesicles from which pus escaped causing the formation of small yellowish crusts, giving the appearance of impetigo. In the center of the inflamed area was a hard tumor, pressure on which caused the escape of pus through a small fistula. A smaller growth was near it. The organism was grown on various mediums and was recovered from experimental lesions in animals. This patient recovered under the administration of potassium iodid. About the same time Steele and Lee [16] isolated a nocardia in the sputum of a patient with pneumonia and empyema. In 1914 Davis [17] reported another pulmonary case. In 1916 Macfie [18] discussed trichonocardiosis, a disease affecting the hair shafts of the axillae and groin. The organism described does not agree in detail with the one from my case, but evidently belongs to the same group. Pijper [19] recovered a nocardia from a case of bronchitis, and reported indifferent results from vaccines. In 1918, de Korte [20] reported a case involving the external ear with a dusky red, brawny swelling extending about 2 inches around the insertion of the ear. The patient ascribed the

14. Wright, J. H.: Nocardiosis, in Osler, Modern Medicine, 1907, p. 340.

15. Potron, M., and Thiry, G.: Pyodermatomycose provoquee par un "Nocardia," Rev. méd. de l'Est **45**:159 and 198, 1913.

16. Steele, A. E.: A Case of Infection with Nocardia, Boston M. & S. J. **169**:502 (Oct. 2) 1913.

17. Davis, D. J.: An Acid-Fast Streptothrix (Nocardia), Chicago Path. Soc. Trans. **9**:177, 1914-1915.

18. Macfie, J. S.: A Fourth Variety of Trichonocardiasis, Ann. Trop. M. & Parasitol. **10**:283, 1916.

19. Pijper, A.: Nocardiosis, Med. J. S. Africa **12**:141, 1916-1917.

20. De Korte, W. E.: Nocardia Cylindracea; a South African Otomycosis, Ann. Trop. Med. & Parasitol. **11**:265, 1917-1918.

Fig. 5.—An old culture.

trouble to a prick on the ear with forage. Iodids caused improvement but did not cure, recourse being had to an autogenous vaccine.

Christopherson [21] reported a case of primary nocardiosis of the lacrimal gland. Other cases are reported in the literature, but the original articles are not available.

I am indebted to Dr. O. Klotz of the Department of Pathology, University of Pittsburgh, for the drawings.

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21. Christopherson, J. B., and Archibald, R. G.: Primary Nocardiosis of the Lacrimal Gland, Lancet **2**:847, 1918.

# THE HISTOGENESIS OF MOLLUSCUM CONTAGIOSUM*

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In a paper by Wile and Kingery, presented at the last annual meeting of the American Dermatological Society, were detailed a series of experiments directed toward a demonstration of the etiologic agent of molluscum contagiosum. As a result of their studies, these authors were able to show that the lesions of this disease can be produced experimentally from the sterile filtrate of molluscum lesions, thereby justifying their conclusion that molluscum contagiosum is caused by a filterable virus. The technic of these experiments, as carried out on themselves and their assistants, was comparatively simple. Molluscum lesions were removed by curettement, ground up in a mortar containing a small amount of sterile saline, and the resultant mash passed through the finest Berkefeld filter under negative pressure. The filtrate thus obtained, which produced no growth on all ordinary culture mediums, was injected intracutaneously into human subjects, at the points of predilection for the development of this disease. After an incubation period varying from twelve days to three weeks, definite papular lesions developed at the sites of the injections. These lesions rapidly took on the clinical characteristics of molluscum contagiosum. Those examined histologically, after a developmental period of eight weeks, presented the unmistakable picture of the disease, including the so-called "molluscum bodies." The subjects of these experiments were under daily observation and histologic study was undertaken at short intervals during the entire evolution of the lesions. In this way material was obtained including every developmental phase of the lesions, from the earliest pinpoint papule, up to the mature stage with its waxy appearance, the central umbilication, etc. The material thus studied offered an unusual opportunity for the investigation of lesions whose histogenesis has been a debated question since the time of Bateman's original description of the disease. It is on a critical examination of this material that the present study is based.

## TWO THEORIES REGARDING ORIGIN OF MOLLUSCUM CONTAGIOSUM

The opposing views of many leading investigators, regarding the peculiar histologic picture presented by molluscum contagiosum, are

* Read before the Section on Dermatology at the Seventy-First Annual Session of the American Medical Association, New Orleans, April, 1920.

found recorded frequently in the literature on this disease. Out of these controversies two preeminent theories have been developed, which are today used in an attempt to explain the origin of these lesions.

*Theory of Pilosebaceous Origin.*—The first of these views to be advanced was to the effect that the lesions of this disease are related to the pilosebaceous apparatus. Engel [1] was among the foremost to take a definite stand on this interesting phase of the question. As the result of a series of observations, he stated his belief that the molluscum tumor was to be regarded as an enlarged sebaceous gland. This view

Fig. 1.—Early pinpoint size experimental lesion, showing beginning localized acanthosis and related gland structures.

was strengthened a few years later, when Virchow [2] published the results of his investigations of this disease. He interpreted the histologic picture as a lobulated glandular epithelioma, arising from the hair follicle. He further likened the molluscum bodies to fat-like

1. Engel: Ztschr. d. k. k. Gesellschaft der Aerzte in Wien **2**:408, 1844; abst. White and Robey: Molluscum Contagiosum, J. Med. Research **7**:25, 1902.

2. Virchow: Molluscum Contagiosum, Berl. med. Gesellschaft Sitzung, Dec., 1864; Berl. klin. Wchnschr. **2**:34, 1865.

globules surrounded by a double-contoured rim, which resisted the action of water and acids. A few years later Kaposi's [3] views were published. He was one of the first to agitate the contagiousness of the disease and at the same time he stated his firm belief in the follicular origin of the tumors. The following year Vidal [4] likewise expressed himself as believing the tumor to be of pilosebaceous origin, and added the suggestion of a colloid degeneration of the cells. The papers of Renaut,[5] Crocker,[6] Hebra,[7] and Benda [8] appeared shortly afterward, in which each, while placing different interpretations on the molluscum bodies, firmly stated his belief that these tumors arise always in connection with the pilosebaceous apparatus. Among the list of supporters of this view must also be included the names of Erasmus Wilson,[9]

Fig. 2.—Experimental molluscum lesion, a few days later; acanthosis more marked.

3. Kaposi: Ueber das sogenannten Molluscum Contagiosum, Vierteljahresschrift f. Dermat. u. Syphilis **4**:333, 1877.

4. Vidal: Soc. de Biol., Seance du 15 juin, 1878, Progres méd. **0**:478, 1878.

5. Renaut: Anatomie pathologique de l'acne varioliforme, Ann. de dermat. et syph. **1**:397, 1880.

6. Crocker: Diseases of the Skin, London, H. K. Lewis, 1893, p. 479.

7. Hebra, F.: Diseases of the Skin, Including the Exanthemata **1**:131, trans. by H. Fagge, London.

8. Benda: Untersuchung ueber die Elemente des Molluscum Contagiosum, Dermatol. Ztschr. **2**:195, 1895.

9. Wilson, E.: Diseases of the Skin, London, 1842, p. 341; ibid.: Diseases of the Skin, Philadelphia, 1863, p. 653.

Rokitansky,[10] Tilbury Fox,[11] Hutchinson [12] and others. Minor differences of opinion are to be found in the publications of these investigators; yet, in the main, it is to them that we owe the belief, still shared by many authorities, that the lesions of this disease are always, in some way, related to the pilosebaceous apparatus of the skin.

*Theory Regarding Origin of Molluscum Contagiosum in Rete Layer of Epidermis.*—Coincident with the studies and investigations mentioned above, however, other and equally reputable investigators placed an entirely different interpretation on the microscopic picture of these tumors. For them the lesions were never related either to the follicles or the sebaceous glands, but were due to a pathology concerning only the rete layer of the epidermis. As early as 1848, only a few years after the article by Engel, von Barensprung [13] described the bodies making up these tumors as epidermal cells which had undergone a peculiar degeneration. He furthermore stated his belief in their nonfollicular origin. A few years later Retzius [14] concluded, after a series of observations, that the tumors were never related to the pilosebaceous apparatus, but owed their origin entirely to the epidermis. Shortly thereafter Boeck,[15] after a careful study, entirely denied the sebaceous origin of the lesions, because fat is never detected in the cells. This reasoning, however, is hardly more tenable than would be a similar objection to the origin and relation of a tumor of the pancreas because of the absence of pancreatin in the cells of such a new growth. The absence of fat might be more easily explained by the changes through which the cells must pass before molluscum bodies are obtained. The papers of Lukomsky [16] and O. Simon [17] then followed, and offered separately, as an explanation, an enormous proliferation of the rete cells, resulting in the peculiar tumor formation seen. A few years later the subject was carefully presented in a paper by Geber,[18] in which

10. Rokitansky: Pathologische Anatomie, Ed. 3, Vienna, Braumuller, **2**: 79, 1856.

11. Fox, T.: Case Report, Clinical Society of London, April, 1872, Brit. M. J. **2**:538, 1872.

12. Hutchinson, J.: Lectures on Clinical Surgery, London, J. and A. Churchill, 1878.

13. Von Barensprung: Beitrage zur Anatomie und Pathologie der Haut, Leipzig, 1848, p. 43.

14. Retzius: Ueber Molluscum Contagiosum, Deutsch. Klin. **23**:450, 1871.

15. Boeck: Ueber Molluscum Contagiosum und die sogenannten "Molluscumkorper," Vierteljahresschrift f. Dermatol. u. Syphilis **2**:23, 1875.

16. Lukomsky: Ueber Molluscum Contagiosum, Virchows Archiv. **65**:145, 1875.

17. Simon, O.: Ueber Molluscum Contagiosum, Vierteljahresschrift f. Dermatol. u. Syphilis **3**:400, 1876.

18. Geber Ein Fall von Epithelioma molluscum (Virchow) universal mit besonderer Rucksicht auf dos Wesen deiser Frankheit Pest, Med. chir. Presse, Budapest, 1882, pp. 685, 703.

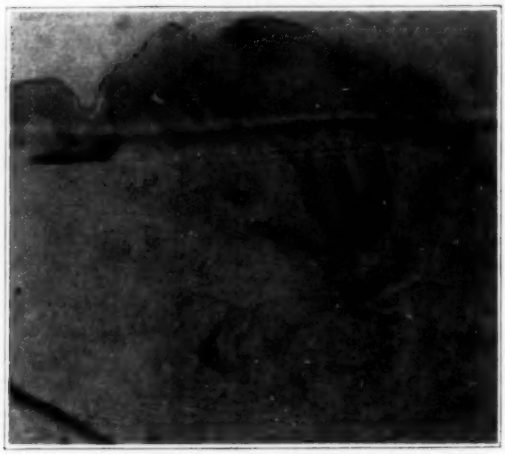

Fig. 3.—Early experimental molluscum lesion, showing involvement of follicle, hair remnants and related gland.

Fig. 4.—Continuation of follicular acanthosis and beginning cellular degeneration.

he attempts to trace the evolution of the rete cells into the molluscum bodies. Still later Neisser,[19] 1882, Stanziale,[20] 1890, and McCallum [21] in 1892, published papers, and among other observations stated their firm belief in the nonfollicular origin of the tumors. In 1896 Unna's [22] histopathology appeared with a most thorough elucidation of the subject. In this Unna suggested the term "epithelioma contagiosum," and stated that he did not believe the tumors to be of sebaceous origin because he had never seen any sebaceous material in the tumor tissue. This reason, however, seems to prove the point no more than that offered by Boeck and is, I believe, open to the same objections. Finally, a most scholarly review of the subject, presenting previous and contemporary opinions, has more recently been published by White and Robey.[23] Besides those mentioned above, the names of Campana,[24] Torok,[25] Klebs and Kromayer [26] must be added to those who believe in the nonfollicular origin of the lesions of the disease.

Such, then, have been the theories of the histogenesis of molluscum contagiosum up to the present time. Two explanations, one almost diametrically opposed to the other, yet each supported by more than one of the leading investigators of their time. Similarly, differences of opinion have arisen through attempts to explain the derivation and origin of the so-called "molluscum bodies." This, and other ques ions, have not been included in the present study, in which the subject of histogenesis only has received consideration. So far as the literature reveals, the opportunity for investigation of material similar to that of the present study has never presented itself in the past. This fact, it is believed, justifies a fairly detailed account of the changes as observed in the development of lesions experimentally produced.

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19. Neisser: Ueber das Epithelioma (sive Molluscum) contagiosum, Vierteljahresschrift f. Dermatol. u. Syphilis **15**:553, 1888.

20. Stanziale: Gior. Internazional de Sc. Med. n. s. 1890, n. s. **12**: 321, 1 pl. Contributo sperimentale anatomo-patologico e batteriologico all studio del mollusco contagioso di Bateman.

21. MacCallum: Histology of Molluscum Contagiosum, J. Cutan. & Gen.-Urin. Dis. **10**:93, 1892.

22. Unna: Histopathology, Diseases of the Skin, Walker's trans., Edinburgh, W. F. Clay, p. 793.

23. White and Robey: Molluscum Contagiosum, J. Med. Research **7**:255, 1902.

24. Campana: Sui globi del Mollusco contagioso, Gior. ital. d. mal. ven. **21**:37, 1886.

25. Torok and Tommasoli: Ueber das Wesen des Epithelioma Contagiosum, Monatsh. f. prakt. Dermat. **10**:149, 1890.

26. Klebs: Psorospermirn im Innern von thierschen Zellen, Virchows Arch. f. path Anat. **16**:188, 1859.

Fig. 5.—Experimental lesion few days older, showing early cavity formation and cellular changes.

Fig. 6.—Experimental lesion, showing epithelial pocket formation, definite papular element and changes, including follicle and gland.

STUDY OF MOLLUSCUM CONTAGIOSUM EXPERIMENTALLY PRODUCED

As stated before, the development of these lesions was under daily observation, so that clinical and histologic examinations were possible as frequently as developmental changes warranted. Approximately twelve days following the injection of the sterile filtrate, one of the patients developed small papular lesions, surrounded by a slightly erythematous zone. These rapidly took on characteristics, making a clinical diagnosis possible. One of several lesions excised at this time are shown in Figures 1 and 2. Apparently, the first change occurring

Fig. 7.—Experimental lesion showing early umbilication, epithelial pocket formation, cellular debris, and related glandular structures.

is that of an extremely small, localized acanthosis, the process resulting in a downward bulging of the epithelium, the increase in thickness being due chiefly to malpighian changes. Apparently, this change continues for some time, the acanthosis becoming more marked, the rete pegs being gradually obliterated, and the process encroaching on the underlying cutis. A few days later, however, serial sections show a factor not present in Figures 1 and 2, i. e., that this acanthotic change involves the follicular wall, a fact evidenced by the hair sheath remnants present and the glandular structures deeper in the section (Fig. 3). Sections a

short time later show a still more extensive involvement of the follicular apparatus (Figs. 4 and 5). The experimental lesions developed fairly rapidly in certain instances, and by the twenty-first day, in one case, had assumed definite papular proportions, presented a waxy appearance, and in not a few a central umbilication was evident. Again serial sections were examined (Figs. 6, 7 and 8). In addition to the

Fig. 8.—More extensive follicular involvement, marked epithelial pocket formation, etc. A lesion clinically typical of molluscum contagiosum.

follicular acanthosis above described, a peculiar cellular degeneration had begun to appear in the central portion of the process. At first these changing cells stain not unlike those undergoing hyperkeratinization. Soon, however, these centrally located, deep-staining cells undergo further degeneration, and in the course of a few days the

process assumes the true outline of molluscum lesions (Figs. 9, 10, 11, 12 and 13). In section, the basal cell layer remains apparently unchanged and intact, and in addition there is epithelial pocket formation with a central cavity containing for the most part cellular debris. Apparently, the so-called molluscum bodies develop relatively late in the disease, as in none of the specimens examined up to this time were the bodies present, although the lesions were clinically typical of the disease. Objective change was gradual from this time on. The lesions slowly increased in size, and one after another, without exception, took on the peculiar waxy color, developed a central umbilication, and from

Fig. 9.—Somewhat later stage, well formed capsule, cellular degeneration, pilosebaceous structures.

time to time the patients complained of pruritis. It was also an interesting observation that new lesions began to appear outside the sites of injection, an occurrence suggestive of the contagiousness of the condition and its dissemination by the trauma incidental to scratching. The lesions at this time were in the sixth week of development, and as the picture had apparently changed so little, biopsies were suspended for a number of days. Approximately eight weeks following the beginning of the experiment, a few more clinically typical lesions developing at the sites of injection, were removed. Sections of these

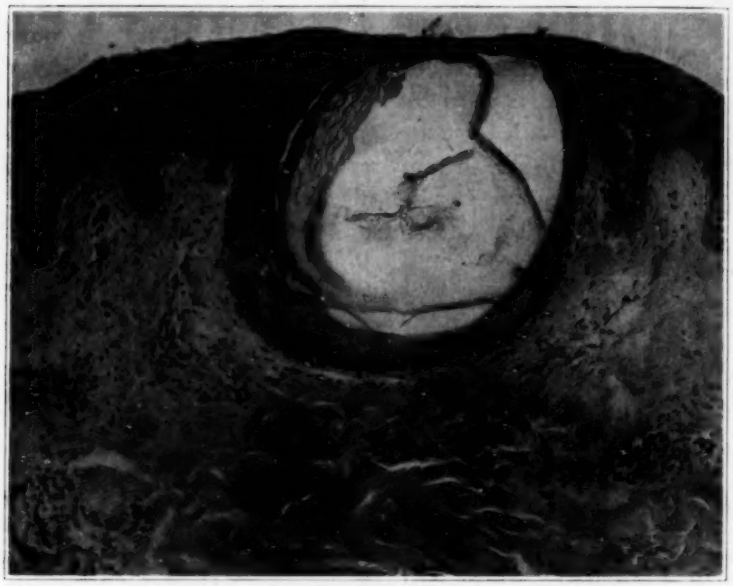

Fig. 10.—Slightly older lesion, showing gradual growth of epithelial pocket.

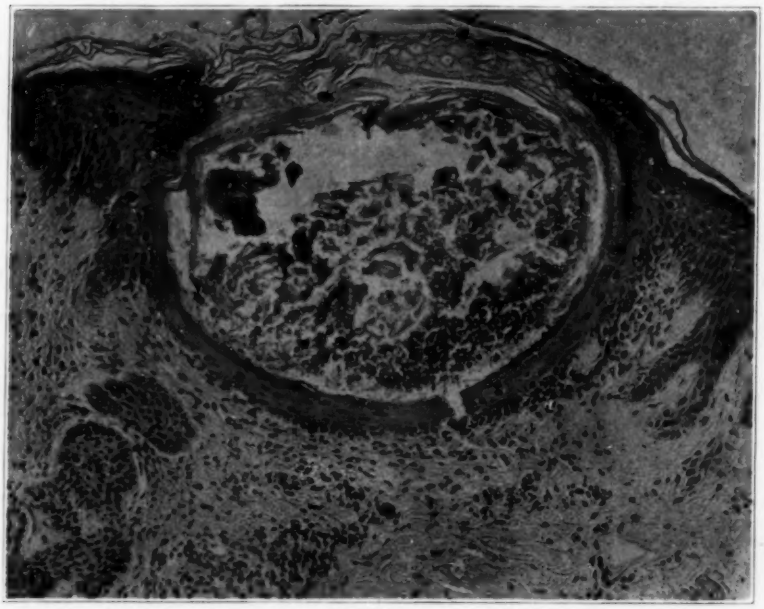

Fig. 11.—Well formed experimental lesion of molluscum contagiosum, typical except for absence of true molluscum bodies.

lesions are shown in Figures 14 and 15. A detailed description of these typical lesions is unnecessary. In Figure 14 the peculiar degeneration of this disease appears below the surface, being attached by an epithelial pedicle of unchanged cells. In the tumor itself, the basal cell layer is apparently little changed, the peculiar metamorphosis becoming more evident as the central portion is approached. The epithelial pedicle extending downward from the surface, in view of the relation shown in previous earlier sections is, I believe, the unaffected portion of the

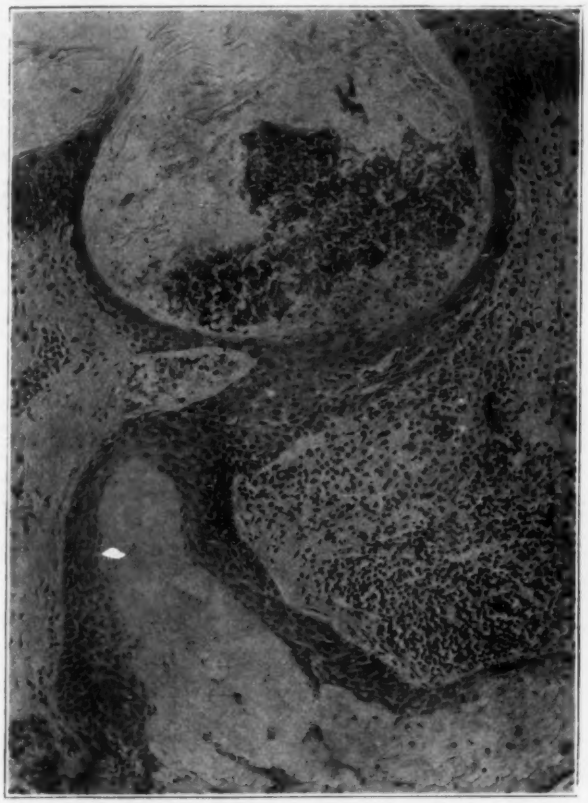

Fig. 12.—Experimental molluscum lesion, showing relation of pilosebaceous apparatus.

follicular wall, in tangential section. In Figure 15, a more central section, the process extends to the surface, umbilication is evident, and the adult stage is evidenced by the presence of the molluscum bodies.

To review briefly, the observations recorded above are from lesions developing at the sites of injections of the sterile filtrate of the lesions of molluscum contagiosum. The described changes are as seen in the

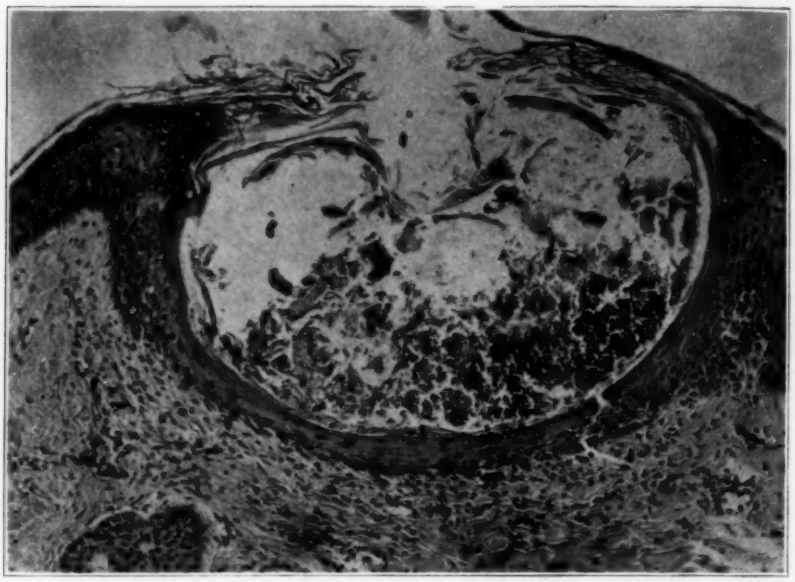

Fig. 13.—Experimental molluscum lesion, approximately six weeks old, the typical picture, lacking only the molluscum bodies, not yet formed, and again showing related pilosebaceous apparatus.

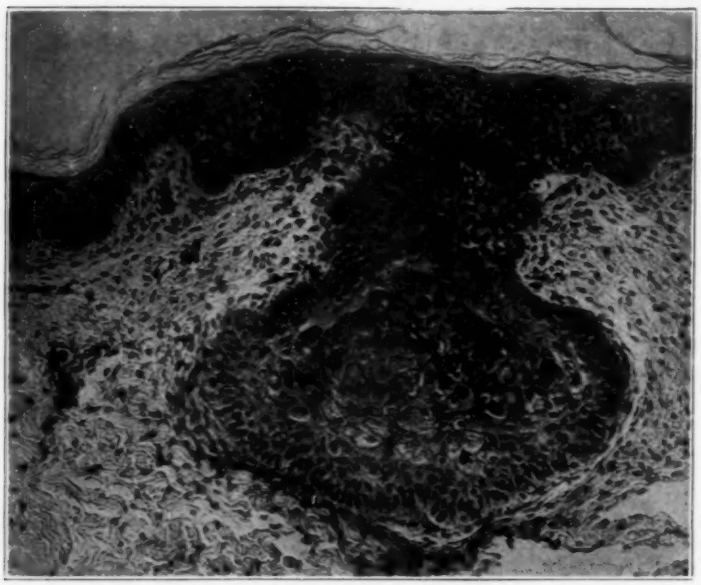

Fig. 14.—Well developed experimental lesion, eight weeks old with epithelial pedicle.

sections, and these, together with the study of many hundreds of sections not reproduced, have continually emphasized a relation with the glandular and follicular structures of the skin.

### STUDY OF SIMILAR DISEASE IN ANIMALS

In spite of this experimental evidence, which is, without exception, in favor of the pilosebaceous origin of the disease, the opinion of those renowned investigators who believed otherwise, cannot be well ignored. Not entirely satisfied, therefore, an investigation of other experimental work suggested itself, with findings worthy of consideration. From time to time, experimental studies and observations have been carried out on a disease, clinically and pathologically identical with molluscum contagiosum of man, occurring in the lower animals.

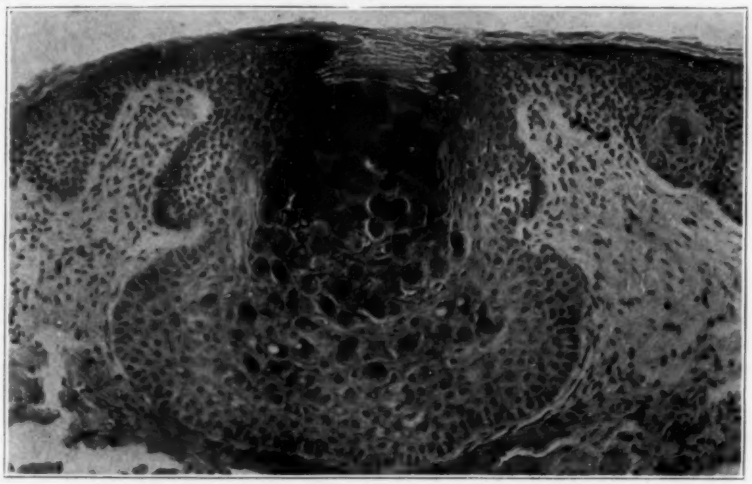

Fig. 15.—Adult lesion a few days older, presenting typical bodies, central umbilication.

As long ago as 1873, Bollinger [27] reported successful inoculations and transplantations in an investigation of the etiology of "Epithelioma Contagiosum" of domestic fowls. He was able to satisfy himself of the contagiousness of the condition, suggested as sites of predilection the comb, wattles, external ears, eyelids and feet of domestic fowls, and lastly he identified the histologic picture with that of molluscum contagiosum of man (Fig. 16). Hutchinson,[28] MacKenzie,[29] and

27. Bollinger: Ueber Epithelioma contagiosum beim Haushahn und die Sogenannten Pocken des Geglugels, Arch. f. path. Anat. u. Physiol. **58**:349, 1873.

28. Hutchinson: Molluscum Contagiosum, etc., Clin. J. **5**:323, 1894-1895.

29. MacKenzie: Molluscum Contagiosum in the Field Sparrow, Canadian Pract. & Rev. (Toronto) **26**:83, 1901.

Fig. 16.—Lesions of "epithelioma contagiosum" occurring on combs, wattles, etc., of domestic fowl.

Fig. 17.—Case of "molluscum contagiosum" involving head and extremities of fowl reported by Fox.

Shattock,[30] a few years later, recorded individual observations of what they termed "molluscum contagiosum in both wild and domestic fowls." In 1898, Colcott Fox [31] presented to the Pathological Society of London, a case of "molluscum contagiosum" occurring in a young fowl (Fig. 17), and called attention to the identity of the clinical and pathologic picture, with that of molluscum contagiosum occurring in the human subject. And lastly, Marx and Sticker,[32] and Mariani,[33] have published the results of separate investigations of "Epithelioma Contagiosum of Fowls." The former were able to produce lesions histologically typical of molluscum contagiosum by rubbing the material from lesions of epithelioma contagiosum into the scarified combs of

Fig. 18.—Section from comb of domestic fowl. Note absence of pilosebaceous structures.

pigeons and chickens. Mariani points out in particular the similarity of the contagiosuness of the two conditions and the identity of the histologic pictures. The foregoing and numerous other references in the

30. Shattock: Molluscum Contagiosum in Two Bunting Sparrows, Trans. Path. Soc. London **49**:394, 1898.

31. Fox, C.: Molluscum Contagiosum of Legs, Feet and Head of the Chicken, Trans. Path. Soc. London **49**:393, 1898.

32. Marx and Sticker: Untersuchungen über das Epithelioma contagiosum des Geflugels, Deutsch. med. Wchnschr. **28**:893, 1902.

33. Mariani: Beitrag zur Aetiologie und Pathologie des Molluscum Contagiosum des Menschen und des Epithelioma Contagiosum der Vogel, Arch. f. Protsitenkunde **21**:213, 1911.

literature leave no doubt that a disease, clinically and pathologically similar to molluscum contagiosum in man, occurs in the lower animals.

In not a few of the above studies certain sites of predilection were emphasized and an investigation of the comparative histology of these parts was undertaken (Figs. 18 and 19). A critical search of serial sections taken from the combs and feet of fowls has in no instance revealed the presence of sebaceous or other glandular structures, nor the suggestion of any analogue. It would seem that this is a point of extreme interest in the light of the interpretations of English investigators; Hutchinson, Fox, MacKenzie, and Shattock, each have reported their observations on what they have elected to term "molluscum con-

Fig. 19.—Section from leg of domestic fowl. Note absence of pilosebaceous structures.

tagiosum" in lower animals. Shattock, in particular, urges the identity of the two conditions, and gives as evidence, besides his microscopic findings, isolated cases of probable transmission of the disease from animals to man. For these investigators, the clinical and pathologic similarity, and the presumptive evidence of transmission, has warranted the use of identical nomenclature. Whether or not these two conditions are identical, as presumptive evidence would lead one to believe; or whether the virus causing these lesions has a certain specificity for the host invaded; are questions that must await the results of future investigations. For the present, one may go only so far as to say that the

analogue of molluscum contagiosum in man does occur in the lower animals, with clinical, pathologic and etiologic characteristics in common. Further, it may be said that the lesions of this disease are capable of developing independent of the pilosebaceous structures.

If we may consider the preexisting theories in the light of the present study, it would appear that each were correct in part. With sections exhibiting but one phase of development, or perhaps obtained from but one case, the reason is patent for previous views having limited themselves to a follicular or nonfollicular origin of the disease. Without doubt, certain cases or at least certain lesions present a pathology which exactly limits itself to the pilosebaceous apparatus. In addition, such a contention may be well supported by the lobulated outline often assumed, the clinical symptom of pruritus, and lastly the ease with which an etiologic agent might gain entrance through the follicular openings of the glaborous skin. To other investigators it may well be that only epithelial changes were evident. There were no glandular structures related in the sections studied and the usual tests for fat, when applied to the so-called molluscum bodies, were negative. If, however, one goes a step further, it may be recalled that embryologically the surface epithelium, the hair follicle and the sebaceous gland and duct have a common anlage. The outer layer of the embryo consists only of ectoderm, from which downward invagination, and subsequent proliferation, result in the pilosebaceous apparatus of the adult, while from the surface portion develops the cutaneous envelope. Embryonically, and we may almost say potentially, therefore, these structures are similar, and given favorable soil, i. e., susceptible individuals, it is but reasonable to believe that the same causative factor may result in changes pathologically similar, whether it be implanted one place or the other.

## CONCLUSIONS

1. Studies by Wile and Kingery have shown the development of experimental lesions of molluscum contagiosum to be limited to pilosebaceous epithelium.

2. An abundance of clinical and pathologic evidence favors the existence of the analogue of molluscum contagiosum in fowls.

3. Absence of pilosebaceous epithelium in the combs and feet of fowls and pigeons, where lesions of molluscum epitheliale often occur, justifies the conclusion that the lesions of this disease can develop independent of pilosebaceous structures.

4. Presumptive evidence points to the identity of molluscum contagiosum in man and molluscum epitheliale in lower animals. Final proof of the development of molluscum contagiosum from the surface

epithelium, therefore, must depend on the establishment of the identity of these two conditions. This identity will be proved only by the successful inoculation of molluscum contagiosum into fowls, and of molluscum epitheliale into human subjects.

5. Experiments directed toward this end have been undertaken in this laboratory.

For the privilege of undertaking this work and for constant and invaluable advice during its completion, I wish to express my indebtedness to Prof. Udo J. Wile.

## ABSTRACT OF DISCUSSION

Dr. J. M. King, Nashville, Tenn.: In 1904 Dr. Crocker of London received a parrot from South America. The bird had papules all over the body, neck and head. The case was diagnosed by Dr. Crocker and Dr. Pernet as molluscum contagiosum. I do not know what the laboratory reported.

Dr. Walter J. Highman, New York: I was taught that molluscum starts in the malpighian rete. The relation of the growth to the pilosebaceous glands is clearly brought out in Dr. Kingery's paper and is quite at variance with the older ideas. Is the disease found in fowls known as "pigeon epithelioma"? Prowazek thought he had found the cause of pigeon epithelioma and he considered the disease closely allied to molluscum contagiosum in man.

Dr. Lyle B. Kingery, Ann Arbor, Mich.: So far as I know, while the investigators believed the disease to be of parasitic origin, they were unable to cultivate or demonstrate a specific organism.

# PROLONGED ICE BOX VERSUS SHORT WATER BATH INCUBATION IN WASSERMANN REACTION *

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The Wassermann reaction is one of the most widely practiced laboratory tests, in spite of its technical shortcomings. It has passed through many stages of evolution, undergone many refinements of technic from time to time, suffered many attempts at its modification, and been lauded and maligned, but it still stands as a monumental aid in the diagnosis, treatment and prognosis of syphilis; however, any further refinement that will increase its efficiency is obviously desirable. The conventional practice of the half hour primary incubation is the phase which I shall call into question at this time, as I believe it to be entirely inadequate and at the bottom of many of the discrepancies between the laboratory and the clinical findings.

The fixation of complement by syphilitic antibody or reagin depends primarily on three factors, namely, the amount of reagin in the quantity of serum, usually 0.1 c.c., the degree of dilution of the serum, and the time allowed for the reaction to take place. Given a serum with a large reagin content and a low dilution, that is, only that degree of dilution which would be brought about by the addition of the other elements of the test, namely, antigen and complement first, and then amboceptor and cells, fixation is instantaneous and requires no primary incubation. If the same serum is diluted, it will be found that the velocity of fixation is in inverse proportion to the degree of dilution.

Now, since the reagin content of serums to be tested in routine Wassermann work is an unknown quantity, and since the routine dilution practiced by many serologists using the original Wassermann system is that involved in bringing the whole up to 2.5 c.c., it follows that the only chance of injecting flexibility into the reaction is in alteration of the time of primary incubation. It is obvious that syphilitic serums with a small reagin content, such as are found in the early, primary and the late tertiary stages of the disease, may, and often do, yield faintly positive or entirely negative results when allotted only thirty minutes' primary incubation in the water bath.

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* Read before the Section on Pathology and Physiology at the Seventy-First Annual Session of the American Medical Association, New Orleans, April, 1920.

* From the Research Laboratory, National Jewish Hospital for Consumptives.

To determine the effect of prolonged primary incubation, a series of Wassermann reactions was examined, both short (one-half hour) and long (twelve hour) periods of primary incubation being employed, and otherwise exactly the same technic to both sets of tests being applied.

Since complement is thermolabile, it is obvious that long periods of incubation cannot be carried out in the water bath, but must be done at low degrees of temperature. The average laboratory refrigerator will maintain a temperature of from 4 to 8 C., while it has been shown that 0 C. gives the best results; my experiments have been carried out at about 6 C., the temperature which the average serologist will find convenient.

## TECHNIC

In the antisheep hemolytic system the native antisheep amboceptor was removed from all serums found to contain it. Each test was performed with five antigens: cholesterinized alcoholic extract of human heart; cholesterinized alcoholic extract of guinea-pig heart; plain alcoholic extract of human heart; plain alcoholic extract of guinea-pig heart, and acetone insoluble lipoids of human heart. Amboceptor titration was performed for each test separately, 0.1 c.c. of the serum to be tested being added to each titration tube. Two units of amboceptor were used in the tests. Complement was pooled from three or more pigs and was used in fixed amount (0.5 c.c., 1:10 dilution); 0.5 c.c. of 2.5 per cent. washed sheep cells; all tubes were brought up to 2.5 c.c. with physiologic sodium chlorid solution. Amboceptor titration tubes for the ice box reactions were set up with the test, with omission of amboceptor and cells which were added and incubated in water bath one-half hour prior to secondary incubation of the test. It was found that the ice box tests usually required one more unit of amboceptor than the water bath.

The results are given in Table 1.

TABLE 1.—Comparison of the Prolonged Ice Box and Short Water Bath Incubation Periods

| | Non-syphilitic | Second Stage | | Third Stage | |
|---|---|---|---|---|---|
| | | Untreated | Treated | Untreated | Treated |
| Total number cases | 72 | 8 | 20 | 18 | 49 |
| Total number positive | 0 | 8 | 10 | 18 | 43 |
| Total number negative | 72 | 0 | 10 | 0 | 6 |
| Positive with both methods | 0 | 8 | 3 | 10 | 18 |
| Negative in water bath, positive in ice box | 0 | 0 | 7 | 8 | 25 |
| Per cent. total positive | ... | 100 | 50 | 100 | 87.7 |
| Per cent. total negative | 100 | ... | 50 | ... | 12.3 |
| Per cent. positive in water bath | ... | 100 | 15 | 55 | 36.7 |
| Per cent. positive in ice box | ... | 100 | 50 | 100 | 87 |

## COMMENT

In this series, unfortunately, there are no primary cases. Of the 167 serums reported, seventy-two were from nonsyphilitic individuals so far as could be determined by history and diagnostic methods;

twenty-eight were from frank secondary cases and sixty-seven from long standing cases, most of which presented positive spinal fluid findings. It will be seen that 100 per cent. of the nonsyphilitic serums gave negative results by both methods. All of the untreated secondary cases yielded positive Wassermann reactions by both methods, while those of this class, both sufficiently and insufficiently treated, showed 15 per cent. positive by the water bath method as against 50 per cent. ice box. This indicates that a large percentage of second stage syphilitics are sent away with a verdict of cured on the strength of the old method Wassermann test, when in fact a longer primary incubation period, of twelve hours of these serums at ice box temperature, would reveal many of them positive and prevent the serious consequence of premature dismissal of such a patient. It is a grave error to advise a third stage suspect that he or she is nonsyphilitic on the strength of a negative Wassermann, when such a serum has been allowed only one-half hour for fixation of complement at water bath temperature. Results on this series of third stage untreated serums reveals this fallacy. This series reveals the discrepancy as entirely technical and in no wise real. Of the eighteen untreated third stage serums, thirteen were from tabetic patients, 100 per cent. of which yielded frankly positive Wassermann reactions by the ice box method of incubation.

As to the serums from the third stage cases under treatment, it will be seen that much the same ratio exists between short and long period incubation results. It is true that the series is not large; but the results are striking and the subject of sufficient interest to warrant this report in the hope that other serologists will extend this study.

A series of spinal fluids from patients with cerebrospinal syphilids were titrated by both methods, with plain alcoholic extract of human heart as antigen. These tests revealed that a positive result is frequently obtained by the prolonged ice box incubation, whereas a negative result is obtained by the conventional water bath incubation period. A typical case is illustrated in Table 2.

TABLE 2.—WASSERMANN REACTION ON SPINAL FLUID OF A PATIENT WITH TABES, INCUBATED BY BOTH METHODS

| Patient R. B. K., Tabes Dorsalis, July 6, 1919 | | |
|---|---|---|
| Quantity of Fluid Used | Water Bath Method ½ Hour Incubation | Ice Box Method 12 Hour Incubation |
| 0.05 | 0 | 0 |
| 0.1 | 0 | 0 |
| 0.2 | 0 | ++++ |
| 0.4 | 0 | ++++ |
| 0.6 | 0 | ++++ |
| 0.8 | 0 | ++++ |
| 1.0 | ++ | ++++ |
| 1.5 | +++ | ++++ |
| 2.0 | ++++ | ++++ |

**SUMMARY**

In the determination of syphilis by means of the Wassermann reaction prolonged, twelve hours, primary ice box incubation possesses decided advantages over the short period, one-half hour, incubator or water bath treatment. Serums giving doubtful reactions by the later method of primary incubation frequently are frankly positive by the former method. In the series studied both methods gave uniformly negative results in 100 per cent. of the clinically nonsyphilitic cases, and positive results in 100 per cent. of the second stage untreated cases. In the second stage treated cases, however, there was a decided difference, especially in the higher percentage positives obtained by the prolonged primary ice box incubation method. Likewise this method gave a decidedly higher percentage of positives in the third stage untreated (attaining 100 per cent. as compared to 55 per cent. by the half-hour water bath method) and the third stage treated cases. In the examination of spinal fluids from patients with cerebrospinal syphilis there frequently is obtained a positive reaction by the prolonged ice box incubation, whereas the conventional water bath method may be negative.

Metropolitan Building.

## ABSTRACT OF DISCUSSION

Dr. John A. Kolmer, Philadelphia: In our studies of the last four years on the standardization of the Wassermann test, we found that primary incubation has required a large amount of work to reach a decision. Our conclusion, based on comparative tests conducted with seventeen different methods of primary incubation, is in favor of the refrigerator method. Our work was conducted with three different kinds of antigens, namely, cholesterinized extracts, plain extracts and extracts of acetone insoluble lipoids. In our experience, from sixteen to eighteen hours at 8 C. results in stronger reactions with all antigens than one hour in the water bath. As to the reasons for these stronger reactions: Our studies have disclosed that complement itself deteriorates to a greater degree in the refrigerator after eighteen hours than in a water bath for one hour. Also more complement is absorbed by antigen alone and serum alone in the refrigerator than in the water bath. Both of these nonspecific factors cause a closer adjustment of the hemolytic system, but there is, also, a greater fixation of complement by mixtures of serum and antigen after eighteen hours at 18 C. than after one hour at 38 C. in either water bath or incubator. Complement fixation tests conducted with the technic of Browning and McKenzie, by which the amount of complement absorbed by serum alone, antigen alone and mixtures of serum and antigen are measured, have shown that more complement is absorbed by mixtures of serum and antigen in the refrigerator at 8 C. than for one hour at 38 C. It is very important, however, to have the hemolytic system suit the method in order to avoid nonspecific reactions. What may be a satisfactory method for the water bath may not be satisfactory for the refrigerator method. A primary incubation of four hours at 8 C., plus one hour in the water bath, gives

admirable results; but it may crowd the day, hence it is better practice to spread the work over two days and conduct the primary incubation for from sixteen to eighteen hours at 8 C. Dr. Burdick, have you compared this refrigerator method with the method you described for testing active serum?

Dr. C. C. Bass, New Orleans: I have been impressed with the fundamental fact that the degree of concentration determines very largely the velocity of antibody reactions. Agglutination reactions may take place in a very short time if fairly concentrated antigen and sufficiently concentrated serum are used. I have not been able to ascertain the optimum primary incubation period in complement binding reactions. I think that any complement binding antisyphilitic serum will bind as much complement in five minutes when there is enough concentration, as it will in much longer time when there is a greater dilution. The same is true in regard to temperature. If the temperature is high, the reaction is rapid. If the temperature is low, the reaction is slower. I have not been able to convince myself that there is the slightest gain in making the Wassermann test by long incubation with greater dilution, over shorter incubation with lower dilution. My own experience has shown that concentrated solutions or concentrated tests in short periods are as dependable as the opposite.

Dr. Ward T. Burdick, Denver: Answering Dr. Kolmer's question, I have not applied the ice box technic to the raw serum method. The method described is of particular importance in the third stage of syphilis. It is very distressing to have a patient, whose physical examination points clearly to syphilis, sent to the laboratory for a Wassermann test and be compelled to return a negative report, as is so often the case. In these cases we have simply not given the reaction sufficient time to take place.

# MALIGNANT DEGENERATION IN BENIGN DERMATOSES *

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The development of malignant neoplasms on dermatoses of the most varied sorts, often of many years' duration, is an occurrence too familiar to all dermatologists to admit of discussion; but to form a just estimate of the dermatoses in which such development is most frequent, to determine the proportion in each class which will probably become malignant, to ascertain the causes which lead to such degeneration — these are more difficult problems and, for the moment at least, insoluble. They are so important, however, especially as our attitude toward them must determine our treatment of many of the so-called precancerous conditions, that an attempt to formulate our present knowledge may be useful.

## PRECANCEROUS DERMATOSES

*Naevi.*—The naevi come first to mind, and it is about the naevi that most has been written in this connection. The vascular naevi may be dismissed at once as no assertion has been made that they are especially prone to malignant degeneration. The case in regard to pigmented naevi is entirely different. There is no questioning the fact that some of these become cancerous, but opinions as to the probability of this occurrence show the greatest divergence. Bloodgood [1] says: "The mole which had become malignant was never a flat pigmented area not elevated above the epidermis, but was distinctly a projecting tumor. It is my opinion that all such moles should be removed, especially when they are in localitites exposed to trauma. Pigmented spots are entirely different." Pusey,[2] on the other hand, says: "The especially dangerous mole is the blue or black mole, which may be slightly elevated or which may, on the other hand, be embedded in the skin and show through only as a bluish black or coal black spot. Malignant degeneration is a very real danger in moles, but so much attention has been given to the possibility lately that the danger of

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* Read before the Section on Dermatology at the Seventy-First Annual Session of the American Medical Association, New Orleans, April, 1920.

1. Bloodgood, J. C.: The Surgical Treatment of Cutaneous Malignant Growths, J. A. M. A. **55**:1615 (Nov. 15) 1910.

2. Pusey, W. A.: Principles and Practice of Dermatology, Ed. 3, New York, D. Appleton & Co., p. 896.

their becoming malignant is, I believe, commonly exaggerated. Malignant growths beginning in moles frequently occur, but when one remembers that hardly an individual lives who has no moles, the relative infrequency of their degeneration becomes evident." Highman [3] even goes so far as to state that "it appears justifiable to eliminate birthmarks from the precancerous dermatoses." There are all shades of differences between these extremes. The general tendency is for the surgeons, who see cases of naevocarcinoma which have become a serious menace to life or even fatal, to incriminate all naevi; while the dermatologists, who see thousands of naevi that remain benign to one that becomes malignant, are naturally more conservative. Pusey's statement is probably nearer the truth than Highman's. We have no statistics to show the proportion of moles that become malignant, no extensive and accurate statistics to show the proportion of cases of cancer which have developed from moles; and even if we had them, these data would not be enough to enable us to solve the problem.

Let us assume, for the sake of argument, that under similar conditions normal skin and naevi have the same tendency to undergo malignant degeneration. If this were true, then on any part of the body — the face, for example — the cancers developing from normal skin should exceed those developing from naevi in the same ratio that the area of normal skin on the face exceeds the area covered by naevi. In that case, the cancers arising on naevi would be a small proportion of the whole, whereas we know that they form a large proportion. Wilson and Kalteyer [4] collected the reports of fifty cases of so-called sarcoma of the skin and found that in 69 per cent. the primary growth had its origin in a mole or naevus, and in some of these traumatism of the mole seemed to act as an exciting cause. They quote Eve's report on melanosarcoma in the London Hospital, who found that of thirty-three cases occurring in the skin, twenty-six began in pigmented moles, and that in a few cases a history of irritation by scratching was obtained. There seems to be no doubt, therefore, that a pigmented mole is more apt than is normal skin to furnish the starting point of this particularly malignant growth; but the danger must be slight, since practically every person has at least one mole, as any surgeon who examined the drafted troops two years ago can testify.

Nearly every observer states that in many or most cases it was possible to obtain a history of repeated slight traumatism before the development of the cancer. It would seem to be reasonable, therefore,

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3. Highman: Precancerous Dermatoses, J. Cancer Res. **1**:343, 1916.

4. Wilson and Kalteyer: Sarcomatosis Cutis, Am. J. Med. Sc. **126**:757 (Nov.) 1903.

to remove all moles which are subject to traumatism — as by the friction of clothes — and to leave the others until they show signs of change by increase of size or by subjective feelings of itching and pricking which would lead to scratching, when operation should be immediate. In practically all cases, the traumatism which seems to lead to malignant change is slight but continuous or at least frequently repeated. A single injury is generally without result. It follows from this that there is no objection to removing a mole by electrolysis or by freezing instead of resorting to operation.

*Recklinghausen's Disease.*—This is so uncommon that it is clinically of little importance. Garré [5] estimates that 12 per cent. of the cases become sarcomatous, and many such cases are recorded. His estimate is probably grossly exaggerated, as it is based on seventeen cases of sarcoma developing in the 150 recorded cases of the disease. The assumption that the 150 recorded cases are any just measure of the prevalence of Recklinghausen's disease is manifestly absurd.

*Xeroderma Pigmentosum.*—The tendency of xeroderma to develop into carcinoma is too well known to require comment. The occurrence of the disease on the exposed parts brings the malignant change in line with the development of keratoses and finally of epithelioma in the skin of persons much exposed to the actinic rays of the sun.

*Senile Keratoma.*—Of the various acquired dermatoses furnishing a starting point for cancer, the most important is undoubtedly the senile keratoma. I have never been able to convince myself that there is any essential difference between this lesion and the seborrheic wart; the "sailor's skin" of Unna belongs in the same class. Here we encounter the same difficulties that beset us in considering the naevi — a multitude of reports of epithelioma which have developed from a keratomatous base, and a great paucity of statistics to show what percentage of these lesions undergo malignant change. The only estimate that I have seen is Hazen's [6] guess that "nearly 5 per cent. of all these keratoses terminate in cancer." He does not state whether he means 5 per cent. of the individual lesions or 5 per cent. of the persons affected — probably the latter — but in view of the extreme frequency of these lesions either estimate seems to me to be exaggerated. Nevertheless, the sequence is so frequent as to be noteworthy, and if any dermatosis deserves the name of "precancerous" it would appear to be this.

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5. Garré: Ueber sekundäre maligne Neurome, Beitr. z. klin. Chir. **9**:465, 1892.

6. Hazen: Skin Cancer, St. Louis, The C. V. Mosby Co., p. 35.

Hyde's [7] articles "On the Influence of Light in the Production of Cancer of the Skin," and McCoy's [8] on "The Solar Keratoses and Cutaneous Cancer" are interesting in this connection. McCoy insists, and justly, on the influence of the actinic rays in producing keratoses, and apparently most of the cases of epithelioma which he had treated had their origin in such apparently benign growths. Sutton's [9] paper on "The Symptomatology and Treatment of Seborrhoeic Keratoses" is most instructive, and in the main points is in accord with the others.

If it be granted that the number of epitheliomas developing on a keratosis is out of all proportion to those arising on normal skin, to what peculiarity of the altered skin are we to assign this susceptibility? It is easy to say that a continuation of the action of the actinic rays which produced the keratosis is sufficient to produce the cancer but, curiously enough, the keratoses are darker than the surrounding skin and are often covered by a crust; they should therefore be better protected against light than the rest of the epidermis, and if the actinic rays are the immediate cause of cancer we should see cancer developing from apparently normal skin rather than from keratoses. It seems probable, therefore, that the actinic rays produce a keratosis and that some other agent induces malignant degeneration. We are still ignorant of what this agent may be.

*Leukoplakia.*—Leukoplakia seems to be closely related to the senile keratomas of the exposed surface, and is due, in most cases, to an irritant acting over a long period of time — such as tobacco or the poison of syphilis. It is a well recognized precursor of cancer, or perhaps it would be more correct to say that most cases of cancer of the mouth develop on the site of a preexisting leukoplakia. The distinction is really important, for cancer of the mouth is rare in comparison with the great frequency of leukoplakia.

*Cutaneous Horns.*—Cutaneous horns form another group of conditions closely related to the seborrheal keratomas from which cancer may arise, but we have no statistics that give any hint of the frequency of this change.

*Syphilis and Tuberculosis.*—Of the various inflammations, syphilis and tuberculosis are probably those which most frequently lead to malignant degeneration. It is in the tongue that syphilis is most apt to be a precursor of cancer, and its influence is probably exerted by first causing ulceration or scar tissue, as in the scar of healed gummas

7. Hyde: On the Influence of Light in the Production of Cancer of the Skin, Am. J. Med. Sc. **131**:1 (Jan.) 1906.

8. McCoy: The Solar Keratoses and Cutaneous Cancer, Arch. Dermat. & Syph. **1**:175 (Feb.) 1920.

9. Sutton, R. L.: The Symptomatology and Treatment of Seborrheic Keratoses, J. A. M. A. **64**:403 (Jan. 30) 1915.

or in the leukoplakias already mentioned. Butlin's [10] statement that "syphilis, in so far as it is capable of producing ulcers and scars of the tongue, so far is it capable of predisposing the tongue to the occurrence of carcinoma" is probably correct. Syphilitic ulcers and scars on other parts of the body do not seem prone to malignant change.

Tuberculosis, in the form of lupus vulgaris, is often mentioned as a possible precancerous condition, but here again it is not the lupus nodule that seems to be the point of origin, but rather the old chronic ulcer. During the past winter I saw a patient at the New York Skin and Cancer Hospital with an ulcerative lupus vulgaris of many years' standing, presenting a large epithelioma growing from a scarred and ulcerated area on the back of the neck, and also a small recent epithelioma developing on a senile keratosis on the right cheek, at some distance from any lupus tissue. I am not aware that this coincidence has been noted before. It suggests the possibility that the unknown cause of cancer — whatever it may be — found in this patient two regions prepared for its action by two separate and distinct causes.

*Lupus Erythematosus.*—This is a much less frequent forerunner of cancer than is lupus vulgaris. In ten cases in which I find the sequence recorded, it was always in the scar tissue that the degeneration began.

*Ulcers.*—Large open ulcers, like those caused by varicose veins, do not often develop into epitheliomas. Lynch [11] has recorded two cases of pellagrous ulcers, sections of which were shown by the microscope to be epithelioma, although the diagnosis could not be made by clinical examination.

*Roentgen-Ray Burns.*—The development of epitheliomas on old roentgen-ray burns is familiar; here again we encounter the familiar sequence — repeated irritation, atrophy, scar tissue, epithelioma.

### CHEMICAL AGENTS PRODUCING CANCER

Among chemical agents with a reputation for producing cancer, two stand preeminent — arsenic and tar, the one acting apparently from within, the other from without; and in each case the development of cancer is preceded by the formation of a keratosis. The problem seems to be reduced, therefore, to the same terms as in the case of senile keratoma: Why and when does a warty growth become cancerous?

In this connection two articles in the *Journal of Cancer Research* for 1918 are most interesting. The first is by Yamagiwa and Ichi-

10. Butlin: Diseases of the Tongue, Ed. 2, 1900, p. 315.

11. Lynch: Epithelioma Developing in a Skin Ulcer in Pellagra, J. Cancer Res. **2**:77 and 131, 1917.

kawa.[12] The investigators conducted a long series of experiments, painting with coal tar the inner surface of the ear of the domestic rabbit, an organ in which spontaneous new growth had never been reported. The alteration in the skin produced by the tar varied from an atypical overgrowth of epithelium to tumors which had the clinical and histologic appearance of cancer. Three of the cases are worth quoting in a little more detail.

In Case 4 of the series, on the two hundred and seventy-third day, the painting with tar was discontinued. At that time there was an ulcer 2.8 cm. in diameter, raised above the skin, with raised edges, resembling a rodent ulcer. A nodule had developed on the outer surface of the ear in a situation corresponding to this growth on the inner surface. The nodule continued to grow after the cessation of the painting with tar, spreading along the surface; the lymph nodes at the root of the ear began to swell, and the animal commenced to lose weight. It died on the three hundred and sixty-sixth day, ninety-five days after the last application of tar—greatly emaciated. The tumor was then twice as large as when the irritant was discontinued. Microscopic examination of a piece of the tumor removed on the two hundred and seventy-third day showed carcinoma in its early stage, while two lymph nodes at the root of the ear and one of the submaxillary nodes showed solid and cystic metastatic nodules, the former consisting of masses of cancer cells, while the walls of the latter were covered with a many-layered epithelium which in many places had formed epithelial pearls and was infiltrating the lymph sinus and the surrounding tissues. Case 6 of the series was similar. The irritant was discontinued on the three hundred and twenty-second day and the animal died on the three hundred and thirty-eighth day, extremely emaciated. The ulcerated tumor and two lymph nodes at the root of the ear had continued to enlarge after the last application of tar. The microscopic findings were similar to those in the preceding case, and the metastatic growth in the lymph nodes was found to be infiltrating the surrounding tissue.

Case 7 of the series is in some ways the most important of all. The irritant was discontinued on the two hundred and fifth day. On the two hundred and eighty-sixth day a diffusely irritated spot on the treated surface began to enlarge, and by the five hundredth day it had produced a cutaneous horn. An ulcer appeared at the base, and on the five hundred and twentieth day the horn fell off, leaving an ulcer with edges raised 0.5 cm. from the surrounding surface and with an even finely granulated base. The ulcer continued to increase in size, and on the five hundred and sixty-fifth day the lymph nodes at the root of the ear began to swell. A fragment removed for microscopic examination had all the characteristics of a rodent ulcer; the epithelium had infiltrated into the lymph vessels and veins and formed a thrombosis of carcinoma cells in them; it had penetrated the ear cartilage and had produced an ulcerated nodule on the outer surface of the ear.

The authors conclude that the repetition or continuation of chronic irritation may cause a precancerous alteration in epithelium previously

12. Yamagiwa and Ichikawa: Experimental Study of the Pathogenesis of Carcinoma, J. Cancer Res. **3**:1 (Jan.) 1918.

normal, and that if the action be continued carcinoma may be the outcome even though no specific agent has been interpolated.

These results may have an entirely different interpretation, however. The repeated applications of tar produced keratosis, and after a time growths which seemed to be true carcinomas appeared; but it is noteworthy that in one case the first clinical evidence of epithelioma appeared about ten months after the discontinuance of the irritation. The tar was the cause of the keratosis; but the malignant degeneration of this keratosis could not be the result of the irritation by tar, as tar was no longer used; it appears rather as if the horn itself were the irritant which induced the change.

Ross,[13] in the same volume, has an article which attacks the problem from an entirely different angle. Studying the occurrence of occupational cancer, he finds that in nearly every case the irritant is chemical, not mechanical. Gritty coal dust does not cause cancer, while soft soot does. Soot, it is to be remembered, is not pure carbon, but contains tar, and tar oils also. The occupations, among the workers in which he finds cancer to prevail, involve exposure to tar, pitch, soot and certain grades of paraffin; kangri cancer he believes is caused by the product of imperfect combustion in the brazier, rather than by the heat; and he calls attention to the frequency of cancer in tissues irritated by tobacco and betel nut, and among farm laborers who frequently handle manure and who show, according to the Registrar-General's returns for 1890-1892, an incidence of eighty-four deaths from cancer as against fifty-one for all occupied males. Broders[14] also finds basal celled epithelium more frequent in farmers than in others. Among the workers in tar and tar products, the especial incidence of cancer is confined to those who handle certain grades of the substance. He points out that all these substances which seem to have a tendency to produce cancer are the products, or are derived from the products, of the death and decomposition of living matter. Examining these substances still further, he finds that they all contain certain compounds which he calls auxetics and which have the property, experimentally proved, of promoting cell division. The coal products which do not seem to produce cancer were found not to contain auxetics. In occupational cancer, therefore, the auxetics, the inducers of cell proliferation, the predisposing cause of cancer, are introduced from without; in senescence, they are produced within the body by the physiologic increase of cell death; in cancer following traumatism, they are produced by local cell injury. It is to be noted, however,

13. Ross, H. C.: Occupational Cancer, J. Cancer Res. **3**:321 (Oct.) 1918.

14. Broders, A. C.: Basal-Cell Epithelioma, J. A. M. A. **72**:856 (March 22) 1919.

that in all these cases of occupational cancer there is first the production of a keratosis, then a malignant degeneration; and evidence is still lacking to show that this final change is the result of the same chemical action as the former.

### IRRITATION COMMON ETIOLOGIC FACTOR

In reviewing these various forerunners of cancer, there is one factor common to all, and that is irritation — usually repeated over a period of months or years. Irritation by chemicals, by actinic rays, by roentgen-rays, by germ action or germ products, all lead to epithelial hyperplasia, or it may be to atrophy and scarring, but the action seems to end there. The keratotic or sclerotic tissue, however produced, is then the starting point of a change of a different order, which we call malignant degeneration. Ribbert [15] states, in concluding his great work, "Das Karzinom des Menschen": "Carcinoma develops on the basis of a subepithelial inflammation caused by epithelial products which decrease the differentiation of the epithelial cells and permit their downgrowth." Although he lays greatest stress on the subepithelial change, he finds the exciting cause in an epithelial product. Apparently, this substance is produced by the altered epithelium of keratosis and of scar tissue more often than by normal epithelium, but we are still ignorant as to why certain keratoses should produce it while others do not. It may be that mechanical irritation will so alter the metabolism of their component cells as to lead to the production of this hypothetical substance, but we do not know.

### SUMMARY

To sum up, there are many causes which lead to keratoses and scars, and keratoses and scars are more prone to malignant degeneration than is normal skin, but the number of keratoses and of scars is so enormous and the number of epitheliomas relatively so small that the danger in each individual case is slight indeed. Our aim should be prophylaxis—to prevent the formation of these precancerous conditions; to watch and protect them when they appear; to remove them when exposed to injury or when they show signs of changing their character. But to recommend the removal of every scar, every naevus, every keratoma, when every person has at least one of these blemishes, or to frighten the public with tales of the menace of such growths, is not justified by the facts.

48 East Forty-Ninth Street.

15. Ribbert: Das Karzinom des Menschen, Bonn, 1911.

# PRODUCTION OF TUMORS IN THE ABSENCE OF PARASITES *

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## VARIETIES OF TUMORS IN PLANTS

There are many kinds of tumors in plants. These are due to a variety of causes which are principally living things—gall flies, plant lice, nematodes, fungi, myxomycetes and bacteria. Tumors may also be due to frost (Harvey), to mechanical irritation (Wolf) and, as I hope to convince you, to a lack of aëration and the resulting increase in acidity of the imperfectly aërated tissues. Clinically, if we may use such a term in speaking of plants, the tumors are either benign or malignant, sometimes grading from one into the other, as in crown gall. Morphologically, they are almost as diverse in appearance as the causes that produce them. Their general structure depends not only on the stimulus received from the parasite, but also on a variety of internal conditions peculiar to the host plant. In other words, the response of the plant varies not only according to the quantity and the quality of the stimulus received, but also according to the age of the plant, the parts attacked, the conditions of nutrition, and various unknown factors, which leads on the one hand to resistance and on the other to increased susceptitbility. The cells composing these tumors may be slow growing and nearly normal in size and orientation as in benign animal tumors, or the tumor may consist of a congeries of small, rapidly dividing, deep staining, disoriented, destructive, anaplastic cells, strongly suggestive of the malignant tumor cells of animals. Every tumor, of course, has its stroma, variable in amount.

What form the tumor takes depends partly on its location; but to a much greater extent on whether the parasites are few or many, whether they are imprisoned in small chambers, as in the case of gall-fly larvae, or are free to move about in the tissue, as in the case of nematodes and bacteria. In the first case, the tumor tissue although hyperplasial approximates the normal tissue in form and arrangement of its cells, because the physical-chemical stimulus always proceeds in the same general direction, i. e., from a central cavity in all direc-

* Read before the Section on Dermatology and Syphilology at the Seventy-First Annual Session of the American Medical Association, New Orleans, April, 1920.

tions toward the periphery; there is, therefore, nothing to lead to disturbed growth and disorientation of cells. On the contrary, in a nematode or bacterial tumor the organisms are able to move about more or less and the chemical-physical stimulus proceeds sometimes from one direction and sometimes from another, leading to a frequently changed direction of growth and to much disorientation of cells. All tumors, so far as they are due to parasites, must be assumed to be due to the chemical-physical action of the by-products of the metabolism of these parasites, just as most communicable diseases are due not to the parasites themselves, but to their toxins. In case of crown gall, therefore, I cannot be properly accused of abandoning my first position, because I have undertaken to show that the parasite acts through its excretions. Diverse as are the tumors of plants due to parasites, I believe that the fundamental chemical-physical phenomena underlying them are much alike, and that the differences we see, when these differences are not due wholly to varying tissue reactions, must result simply from variations in volume, and direction and continuity of the chemical-physical stimulus. This must be true also of the nonparasitic tumors, and eventually I hope to be able to formulate simple general laws applying to all of them.

## EXPERIMENTAL TUMORS IN PLANTS

This paper relates to the experimental production of small benign tumors. It would be of no special interest if it had not grown out of crown-gall studies and did not appear to throw some light on the general phenomena of tumor formation. I have been experimentally interested in crown gall for fifteen years. For those who do not know what has been done, I summarize the leading discoveries made during this time:

In the Department of Agriculture a widely distributed, harmful plant tumor has been demonstrated to be due to a schizomycete. Although no bacteria are demonstrable in sections of this tumor, nevertheless, they are present in it and can be isolated from it by using the methods of the bacteriologist. By pure culture inoculations with the organism, the tumor can be reproduced at will and has been so reproduced hundreds of times. It may also be reproduced by grafting portions on suitable parts of healthy plants. This tumor possesses the power of continuous growth through several generations (Jensen). It is a hyperplasia which often grows rapidly. It contains few or many vessels, depending on whether the inoculated infected tissues are themselves feebly or highly vascular. Often it is imperfectly vascularized and decays early with the production of open wounds which proliferate from their edges. The tumor destroys by crushing or by

invasion. It often develops invasive tumor strands on which are formed secondary tumors which show the structure of the primary tumor. If inoculations are made in the vicinity of groups of totipotent cells (root, shoot or flower rudiments), the tumor which develops is an embryoma, i. e., it is a rapidly developing, disoriented, anaplastic tissue containing dwarfed fragments of various organs having normal cell orientation, but not necessarily normal organ position—they may be upside down in the tumor. Such fragments may also come to the surface or be borne on the surface and grow for a time as dwarfed shoots or other organs which in turn may be invaded by the tumor tissues. Like cancer, if taken early, the tumor may be removed completely; but in later stages of growth it often returns after removal.

The parasite causing this tumor produces ammonia, aldehyd and various acids, and with these substances I have succeeded in causing small hyperplasias in the absence of the parasite; I therefore assume that it is the by-products of the parasite liberated in the tissues which stimulate the normal cells to become tumor cells. These by-products—ammonia, acetic acid, formic acid, etc.—act, I think, by causing cell precipitates which upset respiration and compel the affected cells to rearrange their protoplasm and divide at once or perish. We must suppose that these substances are given off by the bacteria continuously in minute quantities sufficient to stimulate the cells but not enough to kill them.

Following out my theory that disturbed cell respiration is at the bottom of tumor formation, I tried last year to find what results I could obtain in the absence of parasites by limiting the intake of air in various ways, and in each experiment I reached the same result—increased acidity of tissues and the production of small hyperplasias.

I first experimented on the flesh of potato tubers, cutting out rectangular blocks under sterile conditions and hermetically sealing them in test tubes, the blocks resting on wet cotton. The tissues, being alive, continued to absorb water and to respire and transpire. They formed a cork layer over their cut surface and under this layer, as respiration and transpiration became increasingly difficult owing to the saturation of the air and its limited oxygen content, hyperplasias developed, rupturing to the surface. Titrations showed an increased acidity of the tissues. Sometimes these blocks of raw potato flesh developed shoots and roots which soon showed results of asphyxiation and these also bore many small hyperplasias. The tumors themselves rarely developed roots or shoots. Some of the tubes were kept in the dark at room temperature, and others were exposed in bright light to hothouse temperature, but the results were the same. I have been able to obtain in this way only small tumors, since in my potato blocks in sealed tubes the food supply is limited and the air soon exhausted; but

by placing the potato flesh under better growing conditions with occasional renewal of the air, I believe it might be possible to induce the tumors to grow for a considerable period and perhaps to double or treble the size of any I have yet obtained. All of the tubes contained an abundance of water and the air was always saturated.

I obtained the same results, however, from whole tubers lying either in a covered pasteboard box in dry air on my laboratory table, or exposed to the light on the same table in a large open jar. The tubers pushed sprouts, but owing to lack of water these could not develop organs of respiration and transpiration (that is, leaves), and they became much thickened and covered with numerous small hyperplasias, located under wide open stomata. The tissues developing these hyperplasias were gorged with sugar and starch, contained more oxidizing enzymes than normal, and on titration proved to be several times as acid as normal shoots and tubers. Here again I think imperfect respiration led to increased acidity of the tissues and to the development of the tumors.

In a third series of experiments I obtained numerous small tumors from green potato stems in active growth by suddenly destroying the leafy tops, i. e., the respiring and transpiring organs. This immediately stopped the upward movement of a large quantity of aërated water; oxygen hunger and acidity developed and hyperplasias resulted.

Finally, I have repeatedly obtained the same results on the stems of a variety of plants by blocking the lenticels, which are aërating organs (organs both of respiration and transpiration), with Squibb's liquid petrolatum, following the petrolatum experiments of Wisniewski and of Schilling. As soon as the exchange of gases is interfered with, viz., the intake of air and the movement of aërated water to the surface, tumors begin to form under these lenticels.

In crown gall and various other tumors due to parasites the parasite furnishes the acids and other stimuli as a direct result of its metabolism, but the small benign tumors I am describing are not the result of parasitism. The increased acidity probably results from the incomplete combustion of carbohydrates, i. e., from anaërobic cell-respiration due to poor circulation and imperfect aëration, which we know to be a peculiarity of tumors in general, since most of them are poorly vascularized and out of the general circulation.

If, for any reason, conditions such as I have outlined should occur in parts of the animal body, I should expect to see similar phenomena arise in such parts and, the nutrition being more abundant, the tumors might become large. But as most tumors in plants, and especially in the more destructive ones, are the direct result of parasitism, parasites should also be looked for as the cause of rapidly growing, malignant animal tumors. We are forced to the belief that they must be of

parasitic origin unless we are to regard plants and animals as so unlike that no conclusions drawn from the one can be made to apply to the other. Modern biology opposes such an idea.[1] Those who are interested will find this subject treated in more detail with numerous illustrations in my textbook on "Bacterial Diseases of Plants." [2]

SUMMARY

I have produced hyperplasias (1) by the direct application of dilute acids and alkalies to susceptible plant tissues; (2) by the introduction into the tissues of certain foreign organisms (especially the crown gall bacterium which produces acids and alkali in flask cultures and probably also inside the cells as a result of its metabolism), and (3) I can now bring about the same results in the absence of parasites and their products by limiting the intake of oxygen, thus compelling the cells themselves to manufacture the stimulus which leads to the development of hyperplasias. I can conceive of this taking place only as the result of an anaërobic cell respiration acting on the youngest, most active cells of a tissue; but there must be always some oxygen of the air present, otherwise there will be complete asphyxiation of the tissues, as happened in my first experiments. Probably overgrowths due to freezing and to mechanical injuries will also be found to depend on local interference with cell respiration.

The most striking tumors are obtained by inoculatitng the crown gall organism, *Bacterium tumefaciens*. Some of these are simple tumors and others are tumors containing roots and shoots. Some also show the beginning of secondary tumors, and in the embryomas the invasion of tumor tissue into the embryomatous parts (young roots and shoots).

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1. Smith, E. F.: Crown Gall of Plants and Cancer, Science **43**:348 (June 23) 1916.

2. Smith, Erwin F.: Bacterial Diseases of Plants, Philadelphia, W. B. Saunders Company; in press.

# ROENTGEN RAYS OR RADIUM COMBINED WITH EXCISION IN THE TREATMENT OF KELOIDS *

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Keloids or hypertrophied scars are difficult to treat and require much patience on the part of both patient and physician. So far as is known, the roentgen ray and radium are the only two agents which will arrest the disease or cause it to disappear. If these agents are used early when the scar begins to hypertrophy there will probably be no need of combining excision with the radiotherapeutic effect. It is because of the frequent neglect of hypertrophied or growing scars that it is necessary to call attention to these methods of treatment. If the general practitioner, the surgeon and the dermatologist are alert and apply skilfully the roentgen rays and radium to scars that are beginning to show hypertrophy, keloids will almost be eliminated from the field of medicine. It is true that in many instances slight wounds, especially in the colored race, lead to the formation of large keloids and often these cause so little inconvenience to the patient that they are liable to be neglected until they have reached a considerable size. Too often, however, the surgeon recognizes his helplessness and therefore neglects the condition, and the patient, fearing further deformity from treatment, neglects the condition entirely. If we make it more generally known that radium and the roentgen rays will prevent these growing scars and generally cause their disappearance, patients will be more liable to seek assistance. While keloids or hypertrophied scars occur more frequently in the colored race, they are by no means confined to the colored race, and most patients who have come to me for treatment of this condition have been white. The underlying constitutional cause of the formation of keloids I believe is not known, but the exciting causes are known to all the members of this section, and since the exciting cause cannot be prevented, we need give it no consideration; we shall deal only with the neglect of actual keloids. Usually the patient seeks relief because of deformity or for cosmetic reasons, but occasionally pain is a prominent symptom and brings the patient for treatment. In other cases the keloid may cause actual mechanical obstruction, as when they occur on the feet and interfere with the wearing of shoes.

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* Read before the Section on Dermatology and Syphilology at the Seventy-First Annual Meeting of the American Medical Association, New Orleans, April, 1920.

The roentgen rays have long been used in the treatment of keloids, not only by myself but by many others. MacKee has been especially prominent in calling attention to the value of this method of treatment. The early work was done, as most radiotherapy was done early, by fractional and indefinite doses. Even with this indefinite technic some brilliant results have been obtained. Even today with more definite technic, much skill and much keen judgment will be necessary to obtain the best results, for no two cases react in exactly the same way. Generally, the aim should be to produce a progressive atrophy without erythema or destructive effect on the skin or overlying epithelium. The technic will vary considerably with the size or thickness of the keloid, especially in the cases in which the roentgen rays alone are used. The thicker and older keloids will require more filtration and correspond-

Fig. 1.—Appearance of patient Oct. 6, 1919, with a keloid following operation for an enlarged gland. He was given one full dose of roentgen rays Oct. 6, 1919, and excised within a few days. He was treated again with the roentgen rays Oct. 23, 1919; Nov. 29, 1919; Dec. 20, 1919; Jan. 17, 1920, and March 13, 1920. The second photograph was taken Jan. 17, 1920.

ingly longer treatment. In recent cases of hypertrophied scars, in which the scar tissue is still quite young, considerably less treatment and less filtration is necessary. In these mild types one can use to advantage 5 milliamperes of current, 2 millimeters of filter, with a focal distance of 8 inches, a parallel spark of 9 inches, for a period of two minutes. This will give approximately 8/10 of an erythema dose, and will be within safety limits. This treatment can be repeated in three or four weeks. It must be borne in mind that the factors given will vary in value considerably according to the instrument used, and

one must familiarize himself with the value of each particular instrument. In the thicker and older cases of keloid which one is trying to eliminate by the roentgen-ray treatment alone, it is desirable, when possible, to obtain a cross-firing effect. When this is possible, the area to be affected is divided into two or more portals of entry, and the rays so directed through these various fields that the deeper portions of the rays will cross in the deepest portion of the tumor. In these cases it is desirable to use the following technic: 5 milliamperes with 6 millimeters of filter, a focal distance of 8 inches, and a parallel spark of 9 inches for a period of eight minutes.

### TREATMENT BY RADIUM

Radium will give very similar results if used in corresponding doses; that is, in the treatment of keloids one can produce results almost identical with those obtained from the use of the roentgen rays. Plaques or capsules may be used. One should learn the value of the

Fig. 2.—Appearance of a patient June 24, 1919, with a keloid following the pinching of a small papule. It had been burned out with acid but recurred. One dose of roentgen rays was applied June 24, 1919. The keloid was immediately excised and treated July 23, 1919, with 50 mg. of radium in 0.5 mm. of silver, and 2 mm. of rubber, applied one-half hour. Aug. 18, 1919, 100 mg. of radium were applied for one hour, filtered through 0.5 mm. of silver and 1 mm. of rubber. Sept. 29, 1919, 100 mg. of radium were applied for thirty-five minutes, filtered through a 0.5 mm. of silver, and 1 mm. of rubber. Nov. 11, 1919, 100 mg. of radium were applied for half an hour, filtered through 0.5 mm. of silver and 1 mm. of rubber. The second photograph shows his appearance March 22, 1920.

particular specimen that is being used, and it should be used long enough to produce an erythema dose, with a filtration equal to approximately 0.5 mm. of silver. This will eliminate about 98 per cent. of the beta rays. The duration of treatment will vary according to the size of the specimen used and the size of the keloid which is to be treated. In order to use the radium skilfully, the value of the speci-

men over a given area with the filtration above mentioned at a given distance should be known. From this the necessary distance and area can be calculated according to well-known methods. A 50 mg. capsule in 0.5 mm. of silver and 1 mm. of rubber in direct contact will produce an erythema dose in one hour.

### SURGERY COMBINED WITH RADIOTHERAPY

My chief object is to emphasize the value of this combination. It is not new, and is only original in the sense that I have arrived at the conclusion of the value of this treatment, and have been recommending it for a number of years independent of the knowledge that others have been doing likewise. MacKee [1] says in very large keloids it is preferable to ablate, and then apply the roentgen rays as prophylactic. This may be done also in small keloids in order to obtain a perfect cosmetic result. He also says:

> I have never observed a recurrence after roentgen-ray treatment. When one is treating a very large keloid so much radiation is necessary that there is danger of a degeneration or ulceration with secondary carcinoma formation. At any rate, in the very large keloids one often will fail to reduce them absolutely flat with the skin. Therefore, for cosmetic reasons alone it is advisable to excise and then treat.

The method that I have been recommending as a rather routine procedure is the application of the roentgen rays to the keloid area preceding the operation, preferably a few days to two weeks before, and of a dose such as one would give if the rays were to be depended on to remove the keloid. The keloid, or hypertrophied scar, is then carefully excised. This can be done best when there is sufficient loose tissue or skin round about to close the wound without too much stretching, and I believe that the surgeon should excise as nearly as possible to the outline of the keloid and not attempt to excise wide of the area. I have had surgeons unfortunately make a wide incision such as they would make when removing a malignant growth. This extensive excision only increases the area of scar tissue, for even though the keloid is excised, there will always be a scar. The advantage of excision and combined anteoperative and postoperative roentgenotherapy or radiotherapy consists in the reduction of the scar to the level of the skin, and in many instances of a decrease in the total area of the scar. I usually advise a full dose of roentgen rays within a week or ten days after the excision of the scar. The patient is then seen weekly, and if there is any tendency toward recurrence, more treatment must be given. Three or four applications of the rays should be given to guard

1. The Roentgen-Ray Treatment of Skin Diseases, J. A. M. A. **65**:1886 (Nov. 27) 1915.

Fig. 3.—Appearance of patient Jan. 21, 1913, who developed a keloid following a burn when a child. Fourteen fractional doses of roentgen-ray treatment were given between Jan. 21, 1913, and Dec. 22, 1913, each application measuring about half of a skin dose. The second photograph shows her appearance Sept. 9, 1916. The scar is soft and healthy.

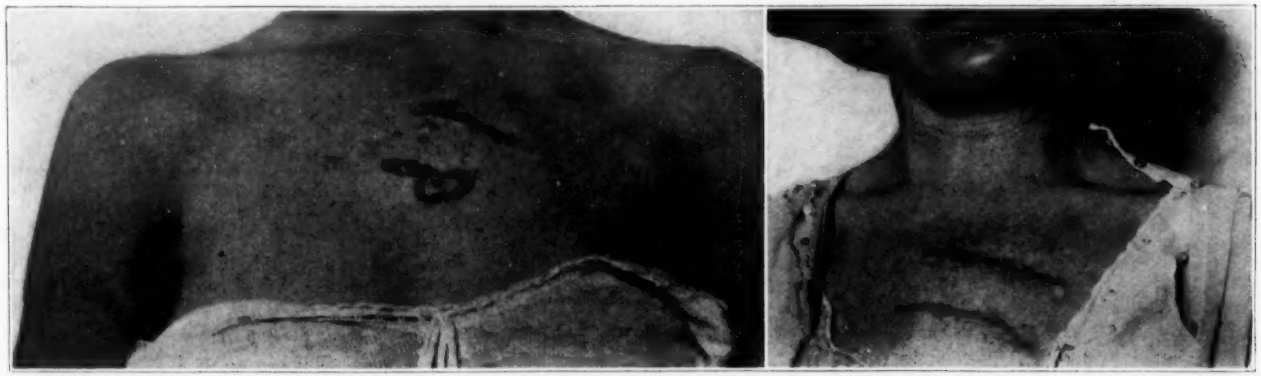

Fig. 4.—Keloid following sunburn; it was treated with the roentgen ray, excised and again given roentgen-ray treatment.

Fig. 5.—Keloid following a burn; treated with nine fractional doses of roentgen rays.

more certainly against a recurrence of the keloid. In several of my cases there has been a tendency toward recurrence following this excision, but in every instance it was thoroughly controlled by either the roentgen rays or radium. In some instances, in which there was localized thickening in the scar, I seemed to get more benefit from the local application of the radium, and this effect seemed to be slightly more positive than when I depended on the roentgen rays.

### CONCLUSIONS

1. Keloids should be treated by radiotherapy as early as the hypertrophy of the scar can be recognized.
2. Radiotherapy can be depended on — either the roentgen rays or radium — for the reduction of a keloid.
3. The best results will generally be obtained when radiotherapy is combined with excision. If applied before and thoroughly after excision, a flat, soft, smooth and inconspicuous scar should be found.

## ABSTRACT OF DISCUSSION

### ON PAPERS OF DRS. WILLIAMS, SMITH AND PFAHLER

DR. NORMAN WALKER, Edinburgh, Scotland: Malignant diseases of the skin have a practical importance in connection with certain industrial processes in our country. The Home Office recently requested that I investigate the distribution of malignant growths in the skin in connection with shale workers. I used to see a bad case occasionally in my time, but I had no idea that the condition was so widespread as it turned out to be. The shale industry gives employment to several thousand men and I had an opportunity of inspecting many of them. Much light may be thrown on the possible cause of these cancers by the investigation of industries. It did not take much investigation to find that we go far too wide when we talk of tar, pitch and paraffin as the causes of these growths. It is possible to pick out the particular kind of work that produces them. The men know this very well. The "green sheds" are the ones that produce these disorders, and wise men refuse to work there, for a large percentage of men working there are afflicted. Men who have worked for twenty-five years may show no irritation. It takes from three to five years to show any irritation, and usually it is seven or eight years before malignancy develops. These growths are of the type of senile keratoses and the patients, as a rule, do not see the doctor about them. They have learned that the application of crude hydrochloric acid is sufficient to cure them. The men who have worked in shale for a number of years are scarred all over with the lesions they have removed. In some instances the growths spread to the glands and kill the patient. The interesting point is that in this particular industry the lesions are limited to the arms and legs, which are exposed. All sorts of precautions are resorted to by the men. If they smear their arms with castor oil before going in, the risk of irritation is greatly decreased. I also inspected the briquet industry in Cardiff, where they mix coal dust with pitch. A great many of the workers had growths, but they were not at all like the paraffin growths. They were found occasionally on the hands and on the scrotum. The most remarkable finding was their presence on the neck. Further, most of them presented

a remarkable sensitiveness to light. One man told me that he felt so much agony on a sunny day that on sunny holidays he retired to his coal cellar where it was perfectly dark, in order to get relief from the pain. About three months ago a man walked into my clinic with a malignant tumor on his hand and other keratotic lesions. He was employed in mending fishing nets. There were only four lesions and two had cancers caused from the tar which was used on the material in the nets. There are three types, the tar, the pitch and the oil cases. These cases are evidently due to certain peculiarities in the skin of the person. About 25 per cent. of the men in the green sheds were affected, a much smaller percentage of the pitch workers and a much larger percentage of the tar workers. A Belgian doctor told me that in the Brussels briquet works during the war there was a great deal of carcinoma, affecting 50 per cent. of the workers. These cases are very much like some of the roentgen-ray cancers and the cancers that sailors and other outdoor workers have. Epithelioma of the lower lip is practically never dealt with by dermatologists in our country. We send these cases to the surgeon. Everyone is agreed as to the importance of early diagnosis.

Hebra is reported to have had four cases of lupus carcinoma. I have had four in my wards at one time. In the early years of roentgen-ray treatment, we had cases of lupus from all over the country. Like everybody else, we did not know its dangers and gave doses which would be regarded as criminal now and the number of those patients who have developed carcinoma since that time is appalling. I think I have had between fifty and sixty cases of lupus carcinoma from this cause. If the patients could all be kept under observation one would not need to worry. I have operated at least twenty times in one case for the removal of carcinoma. But when one gets people of moderate intelligence, who know the dangers, and after having had one roentgen-ray cancer removed come up a few years later with a growth the size of a walnut, it makes me consider very seriously whether we ought to advise roentgen rays in the treatment of lupus. Where it has developed, the dermatologist can manage it better than the surgeon. The prognosis is bad enough, but all patients I have seen and operated on have lived some years, and some of them many years.

As to keloid, I have always been of the impression that excision is the worst possible treatment, but I have not tried excision in connection with roentgen-ray treatment. I have come to regard radium as the proper thing for these cases. Where it was not available I have had excellent results from carbon dioxid snow.

Dr. William Carpenter MacCarty, Rochester, Minn.: Many men working on epithelioma lay more stress on tobacco as an etiologic factor. My associate, Dr. Broders, recently published a very interesting study of epithelioma, in which he adheres to the probability that tobacco plays a rôle. Very little is ever said about the effect of sunburn. Having studied the skin of a few thousand farmers in the Northwest, who are exposed to the sun, and after studying epithelioma in many of them, I believe that sunburn plays an enormous part in the development of these growths, perhaps even a greater rôle than does tobacco. The lips of the farmers are always sunburned in the location in which epithelioma is most common. In my experience, epithelioma arises usually from the outer portion of the lip and not inside next the gum. Almost daily, in our clinic, patients, their relatives, nurses and physicians come in to inquire whether or not to have a mole removed, and I advise against this procedure unless the mole presents some

definite change or is in a location subject to frequent injury. Speaking of epithelioma as types, Dr. Broders has shown that a single epithelioma may contain prickle cells, a glandular arrangement of the cells, and often a squamous epithelioma, frequently in the same section, so I do not believe that a basal cell epithelioma is as much of a type as we have thought. In connection with carcinoma of the stomach I found that the patients who had been operated on and had an advanced degree of differentiation of cells lived much longer than the patients with no differentiation. An epithelial pearl is the result of a high degree of differentiation.

Dr. Smith's contributions to the subject of neoplasia are, perhaps, the most valuable that have ever been made. I believe, firmly, that the secret of cancer will be found by a biologist and not by a pathologist.

Dr. John E. Lane, New Haven, Conn.: It was intimated that we might abandon surgical procedures for cancer of the lower lip in cases in which metastasis has begun, the question being asked whether radiotherapy might not be as effective as ablation. While there has been great improvement in the technic of radiotherapy recently and in the results of it in carcinoma, it seems to me that in the present state of our knowledge we must answer that question with an emphatic "No." For the present the best procedure appears to be ablation followed by radiotherapy. Radiotherapy should not be neglected in inoperable cases, as there is frequently a good chance of arresting the progress of the disease for a time and an occasional unexpected cure is made. Dr. Williams' position as to the removal of moles is sane and conservative. In case of the deeply pigmented moles, however, it would seem wise to excise them or destroy them with the cautery whenever possible. It is frequently too late to save the patient's life after such moles begin to show signs of activity. I can see no point to Dr. MacCarty's advice to patients not to have moles removed. If moles are an annoyance for any reason, even that of unsightliness, I can see no objection to removing them. It can be done without much scarring and there are practically no ill effects from their removal.

Dr. Augustus Ravogli, Cincinnati: The small growths which seem to be entirely insignificant and which last sometimes for one or two years without producing any trouble are often the beginning of an epithelioma, and do not presage anything less than the fight of the cells against the entrance of the periblastic element. When the cancer is present in the epidermis, we have epithelial cells of pathogenic nature making their way into the tissues of the derma. The normal cells put themselves on the defensive to stop the invasion of the heteroplasic cells. This forms a kind of pearl, as we term it. When the cells begin to get down into the corium and the derma, the collaginous textures try to involve these cells, and they form the alveoli, which contain some of the large epithelial cells which constitute the exact features of the cancer of the skin. It is merely an effort of the living organism to stop the progress of these cells. I have seen this epithelial infiltration go deep into the ducts of the sweat glands and invade the coil glands and from there invade the other tissues of the deep corium. The epithelioma following the roentgen-ray burn is the result of a parasitic infection. A few years ago I exhibited a case of cancer en cuirasse. The growth extended over the whole breast. It was the consequence of a burn from roentgen rays.

As to the keratoses and precancerous conditions, I do not see any difference between them, except that the cells are limited to the epidermis. When these cells have a chance to invade the corium, cancer follows. The bite of an insect or any irritation in the vegetable world is capable of causing tumor, just as in the animal tissues.

Dr. William H. Guy, Pittsburgh: The results reported, excellent though they are, should not be contrasted with statistics that surgeons furnish. The greater number of men who are doing this work have come to the conclusion that any one may obtain as good or better results with radium and roentgen rays than with surgery, regardless of whether or not neighboring metastases have occurred. Because of poor surgical results, most careful surgeons refer these cases for radiotherapy alone or combined with surgery either as a preoperative or a postoperative procedure. Some of the previous speakers have mentioned the bad results from roentgen rays, in contradistinction to those obtained with radium. In the smaller type of growth these bad results can be obviated by screening with lead up to the margin of the growth, so that the roentgen ray does not fall on any but diseased tissue. I believe that as good or better results can be obtained with radium, because a smaller dose can be applied and because we are shooting with a rifle instead of with a shotgun, and the radiation from the gamma ray will reach to the greatest possible extent the depth of the lesion. I understood Dr. Pfahler to say that he recommends excision only in the larger growths, and I agree with him. In the not too extensive case one may obtain just as good results without excision, except that a considerable amount of time may be necessary to obtain that result.

Dr. J. M. King, Nashville, Tenn.: I have seen a few cases of carcinoma of the face completely relieved by extirpation of the glands, followed by roentgen-ray treatment. I have removed some keloids and followed the excision with the roentgen rays, with very good results. I have treated some keloids on the face one inch thick with a screened Coolidge tube and have obtained excellent results. Extirpation would probably have resulted in worse scarring than from the roentgen ray alone. I had a patient who when 19 years of age was stung by a wasp on a mole just below his left eye. This soon developed into a carcinoma. When he was about 21, the growth was about the size of a quarter of a dollar. The acid from this sting might have been the etiologic factor in this case. Many more carcinomas are found in the stomach and about the cervix uteri than in any other part of the body. Perhaps some acid substance excites the production of the cancerous cell.

Dr. Richard L. Sutton, Kansas City, Mo.: About eight years ago, Dr. Lain first spoke to me about his method of clinical classification, a plan which has recently been worked out pathologically, and in a most admirable manner, by Broders. At that time, I had always been firmly of the belief that all cases of squamous cell carcinoma of the lip should go to the surgeon first, and afterward to the radiotherapist. Dr. Lain succeeded in convincing me, however, that many of these cases, especially if taken early, can be cured by radium and the roentgen ray. Hazen and Bloodgood have shown that the majority of carcinomas in this region are of the prickle or squamous cell type. Seborrheic keratoses should be divided into three distinct groups: (1) keratoses of the nevoid type, (2) keratoses of the verrucose type, and (3) keratoses of the keratoid type. The last named is the most dangerous of the three. This is the type to which Dr. Hazen ascribes the high percentage of malignancy. The point brought out by Dr. McCarty is important. In my opinion, tobacco

plays an important part in the causation of these lesions. Frost bite also is a prominent predisposing factor in some instances. With regard to the treatment of keloid, Dr. Pfahler's suggestion is a good one, and I shall give it a trial. In combating the smaller lesions, carbon dioxid snow is a valuable agent, as Pusey, Norman Walker and others have shown.

Dr. Harold N. Cole, Cleveland: Tobacco has been largely responsible for carcinomas around the mouth. These growths rarely occur in women. Perhaps in the next generation we shall see more since so many women now smoke.

Dr. William C. MacCarty, Rochester, Minn.: I did not intend to say that tobacco has nothing to do with the production of epithelioma, but that I believed that sunburn was also an important factor, and that when we know the truth we may find out that it is more important than tobacco. I dare say that 75 per cent. of the people in this room use tobacco in some form, but probably none of us has an epithelioma of the lip.

Dr. Howard Morrow, San Francisco: We might divide these carcinomas of the lower lip into the deeply infiltrated and those without much infiltration. I do not think it matters whether the superficial ones are treated with radium, roentgen rays or proper excision. Superficial carcinomas should not be treated by any other methods than those mentioned. Treatment with liquid air and other caustics is still mentioned in many textbooks, but we should not adopt this form of treatment, because it is dangerous. I have had many cases of keloid treated by excision and subsequently by radium therapy and the results have been most gratifying.

Dr. George E. Pfahler, Philadelphia: I have succeeded in curing practically every one of 100 patients with epithelioma of the lip who did not have any metastases in the glands, and who had not been treated previously by caustics or surgical incision. No other treatment can equal that result. The treatment has been, as a rule, the local electrocoagulation of all areas of the disease, including about one-eighth inch around the growth, by means of the high frequency current. I then treat the lip area and the glandular area, usually with the roentgen rays. The same result can be accomplished with radium if you have enough of it, and in none of these cases have metastases developed in the glands. The diagnosis could not be questioned.

When metastases were present in the glands, I have asked the surgeon to excise them and then I treat the whole area thoroughly with deep roentgen-ray therapy. Recently I began to treat a few patients by the introduction of radium needles into these metastatic tumors. I would like to see Dr. Smith carry on the study of irritation. I believe we would learn a great deal about the histology and development of these tumors, and about the effects of radium.

Dr. Everett S. Lain, Oklahoma City: I was pleased to know that the etiologic factors as recorded from larger numbers of patients closely correspond to my own findings. Most of the lower lip cancer patients are those who are out in the open air and are subjected to sunburn. Most frequently they are thin skinned blonds. I am certain that sunlgiht is a predisposing factor in a large number of the cases as well as the use of tobacco. My technic was very uncertain in the early years. In recent years I have most frequently begun by using the beta and gamma rays for the first and perhaps second series of treatments. Later I use only the hard or gamma rays whether or not there is deep glandular involvement. A similar routine has been practiced in the use of roentgen rays. I have been giving one or more series of crossfire, deep roentgen-ray treatments in all cases of suspected glandular

involvement, screening with 3 or 4 mm. of aluminum. Only five of my patients were women and two of these were smokers.

Dr. Charles M. Williams, New York: Classifying lip cancers into those that are readily cured and those that are more malignant will be a great help in selecting the proper treatment. Kangri cancer is believed to be caused by heat, although Ross is of the opinion that the soot and smoke are the important causative factors.

Dr. Earl D. Crutchfield, Galveston, Tex.: There is a distinct basal cell type of cancer which may clinically be considered a nonmalignant growth. The differentiation of prickle cell carcinoma and basal cell carcinoma is simply one of definition. I have seen two cases, both of the basal cell type, and the gland metastases were of the squamous cell type. Pearls are not more malignant, but in many of the rapidly growing types and the rapidly infiltrating types there is a tendency toward degeneration of the epithelium. On the other hand, many of these tumors show no pearl formation. I think the stage in which the cells divide has much to do with classification.

Dr. Erwin F. Smith, Washington, D. C.: All I have wished to do all these years was to get the oncologists to see things in a new light and not depend chiefly on section cutting, not that I deprecate that, but that I conceive something more and different to be necessary. If I can wake them up to that, I think I have done my share of work even if I do not make any animal experimentation. Already cancer specialists have begun to study crown gall from their own standpoint, not only in the United States, but also in England, Germany and other countries, and C. O. Jensen of Copenhagen, is on record as saying: "I fully share the opinion of Erwin F. Smith that crown gall is a new formation which (irrespective of its cause) can be placed side by side with the real malignant tumor formation in the higher animals."

# THE EFFECT OF MERCURY SALICYLATE ON THE WASSERMANN REACTION

## OBSERVATIONS ON THE SEROLOGY OF EIGHTY-SEVEN PREVIOUSLY UNTREATED MEN

HERMAN GOODMAN, B.S., M.D.

NEW YORK

I have recently had the opportunity of treating a number of syphilitic patients solely by the intramuscular injections of mercury salicylate. The paucity of reports of the effect of this drug alone on the Wassermann reaction is deemed sufficient reason for the publication of this study.

### TREATMENT OF SOLDIERS WITH MERCURY SALICYLATE

The eighty-seven patients were men in the military service who had no active manifestations of syphilis. They had all passed the clinical examination of the draft board and that of the enlisting officers. Some of the patients were selected by the routine serologic examination of cooks and bakers, and candidates for these positions.[1] Thirteen of the patients denied having had syphilis. Twelve of these gave a 4 plus Wassermann reaction on more than one examination; the other presented a scar on the penis and scars of bilateral suppurative adenitis. One of the patients was an hereditary syphilitic.

No case in which the patient received arsphenamin previously or concomitantly with the mercury injections is reported in this paper, nor cases in which patients had received previous systemic antisyphilitic treatment as civilians. I am, therefore, unable to report the action of mercury salicylate on the Wassermann reaction in active syphilis. I did not feel justified in withholding from patients with active manifestations of syphilis the chemotherapeutic drug arsphenamin.

The serology was performed at the laboratory of the Institute of Tropical Medicine and Hygiene, San Juan, P. R. The only information the laboratory received was the infirmary number of the patient. The tests were made in duplicate. A clinical control, known positive, was always sent in, and the laboratory had no means of identifying this control. Not infrequently, and with the knowledge of the laboratory director that it was being done, two tests of the same patient,

1. Goodman, H.: Genital Defects and Venereal Diseases Among the Porto Rican Draft Troops, J. A. M. A. **72**:907 (March 29) 1919.

taken at the same time, were put through on the same day, one test by name and the other by number. This ruse, as it might be called, was an impetus to the clerical and technical force which assured me that few, if any, errors of disinterest would occur. In all I was able to correlate the serologic and clinical findings in over 2,500 patients, and I am assured that the tests are trustworthy and do not hesitate to base conclusions on them.

### METHOD OF PROCEDURE

The patients who were given the mercury salicylate treatment had the Wassermann reaction performed at the first visit. Subsequently, for six or eight weeks, they received 1 grain of mercury salicylate in liquid petrolatum. The 10 per cent. suspension was prepared by my pharmacist under the most strict aseptic precautions. The site of injection was the region of the buttock, alternating from one side to the other. Extra long needles were used, sharpened and sterilized after each injection. The Luer all-glass syringe was employed. The dose was not increased progressively. After a course, another Wassermann test was taken, and then a rest of four weeks with freedom from treatment was given. I had planned to have another Wassermann test made before resuming treatment, but few of the patients reported received this test as the demobilization intervened.

### RESULTS

Forty-seven patients showed no change from 4 plus or 3 plus positive reactions after the first course of mercury salicylate. In five patients the Wassermann advanced from 3 plus to 4 plus. In seven patients the reaction was reduced from 4 plus to 3 plus. There were in all fifty-eight patients, or 66 per cent. with minor or no change from very strongly and strongly positive reactions. In one patient there was a reduction from 3 plus to 2 plus. In five cases there was recorded a diminution from 4 plus to 2 plus. In four other cases there was a change from 4 plus to doubtful.

In eight patients, or 9 per cent. of the total, there was a reversal of the Wassermann reaction from 4 plus to negative. In four others the negative Wassermann did not persist, and a 4 plus Wassermann reaction was obtained after the rest period. In one instance the Wassermann 4 plus prior to and at the end of the first course of mercury salicylate was negative at the expiration of the rest period.

The table contains data on twenty-nine cases. Those with no change in reaction have been omitted.

MERCURY SALICYLATE AND THE WASSERMANN REACTION *

| Number | Case | Infected | First Wassermann Test | Number Mercury Salicylate | Second Wassermann Test | Wassermann Test after Rest |
|---|---|---|---|---|---|---|
| 1 | 467 | 1912 | +++ | 6 | ++ | |
| 2 | 632 | Cook | ++++ | 9 | ++ | |
| 3 | 636 | 1918 | ++++ | 8 | ++ | |
| 4 | 395 | 1916 | ++++ | 8 | ++ | |
| 5 | 469 | 1916 | ++++ | 8 | ++ | |
| 6 | 910 | 1915 | ++++ | 8 | ++ | |
| 7 | 746 | 1916 | ++++ | 9 | ++ | |
| 8 | 738 | 1918 | ++++ | 6 | ± | |
| 9 | 1289 | Denied | ++++ | 6 | ± | |
| 10 | 1164 | 1911 | ++++ | 6 | ± | |
| 11 | 1056 | Baker | ++++ | 9 | — | |
| 12 | 1009 | Baker | ++++ | 7 | — | |
| 13 | 1272 | 1916 | ++++ | 5 | — | |
| 14 | 77 | 1916 | +++ | 8 | — | |
| 14 | Continued | .... | ..... | 8 | — | |
| 15 | 388 | 1908 | ++++ | 6 | — | — |
| 16 | 140 | 1912 | ++++ | 7 | — | |
| 17 | 615 | Cook | ++++ | 8 | — | |
| 18 | 102 | 1918 | ++++ | 8 | — | |
| 19 | 263 | 1910 | ++++ | 8 | — | |
| 20 | 187 | Denied | ++++ | 6 | — | ++++ |
| 21 | 392 | 1913 | ++++ | 11 | — | ++++ |
| 22 | 205 | 1915 | ++++ | 8 | — | ++++ |
| 23 | 181 | 1910 | ++++ | 8 | — | |
| 23 | Continued | .... | ..... | 8 | ++++ | |
| 24 | 658 | 1911 | ++++ | 6 | ± | |
| 24 | Continued | .... | ..... | 4 | ++++ | |
| 25 | 186 | 1918 | ++++ | 8 | — | ++ |
| 26 | 502 | 1913 | ++++ | 8 | ++ | |
| 26 | Continued | .... | ..... | 4 | — | |
| 27 | 335 | 1909 | ++++ | 8 | ++ | |
| 27 | Continued | .... | ..... | 5 | ± | |
| 28 | 91 | 1909 | ++++ | 7 | ++++ | |
| 28 | Continued | .... | ..... | 6 | — | |
| 29 | 250 | 1913 | ++++ | 8 | ++++ | — |

* My copy of the history of cooks and bakers does not contain any notes concerning date of infection.

## LITERATURE ON TREATMENT OF SYPHILIS WITH MERCURY SALICYLATE

Although the literature is replete with articles on the use of mercury salicylate in the treatment of syphilis, they are for the most part from the pre-Wassermann period. Many, since the introduction of the reaction, deal with the technic of the intramuscular injection, and methods of rendering it less painful or even painless. Nelson and Anderson,[2] however, reported in 1915 on the use of mercury salicylate in syphilis. The Wassermann tests were made by Craig, and the results were 2 plus, plus, doubtful and negative. The patients in a military prison had not received any previous therapy. There were forty-three latent and seven secondary cases of syphilis. The dose of mercury salicylate was 1½ grains once a week in the beginning, then once in fourteen days, and later irregularly. No patient was salivated; they were all kept at work; few complained of sore buttocks, and there

2. Nelson, K., and Anderson, E. A.: The Use of Mercury Salicylate in Syphilis, with a Record of Its Influence on the Wassermann Reaction in Fifty Cases, J. A. M. A. **65**:1905 (Nov. 27) 1915.

was no objection on the part of the men to the form of therapy. Of the action of mercury salicylate, these authors are of the opinion that: "In the light of our experience it seems improbable that the salicylate alone and unaided possesses any real curative value in this disease. . . . Serum reactions have in some cases varied from double plus to plus minus or minus, and later returned to the double plus while the treatment was in progress. It is our opinion that these variations in the serum reaction are due to other causes than the treatment. . . . It is certainly fair to believe that mercury salicylate used hypodermically in full doses over many weeks of time has little if any real influence on the disease."

These authors give a table of their fifty cases with the Wassermann reaction reported for each month the men were under treatment. The number of injections vary between twelve and twenty; the number of Wassermann reactions varies between six and eight. Two patients gave "two and three negative serum reactions. In both cases the men obtained clemency and were discharged from the prison at this period of treatment and we were unable to follow them further. It is our belief that a continued record on these two cases would undoubtedly have shown a positive reaction later in the treatment. Had they failed to do so they would have been the first to record this, for just this thing did occur in ten cases. This also clearly establishes the value of more than one serum reaction and the error that would arise from the acceptance of a single negative result as final."

Best [3] gave larger doses than Nelson and Anderson, and at weekly intervals. He writes, "the intramuscular injection of mercury salicylate offers the most convenient, most easily controlled, most efficient, and most satisfactory of any of the various forms of mercury treatment." The ten cases he cites do not, however, compare with those of Nelson and Anderson or those recorded in this paper, because seven of the patients had received previous arsphenamin therapy, and all had taken iodids.

Haller [4] reported a group of twenty-five patients in various stages and of various age of infection with 4 plus Wassermann reactions who were treated with mercury until the Wassermann reaction became negative. Treatment was discontinued until the reaction again became positive (4 plus). The average length of time until this occurred was about one month. The extreme case on the one hand was ten days, on the other hand four months. The more active the case, the

3. Best: Intramuscular Injection of Mercury Salicylate in the Treatment of Syphilis, Med. Rec. **89**:473, 1916.

4. Haller, David: Variations in the Strength of Positive Wassermann Reactions in Cases of Untreated Syphilis, J. A. M. A. **66**:882, 1916.

more readily the reaction returned 4 plus, as one would naturally expect. The age of the infection seemed to make little difference in the rapidity of the return to positive. Variations from month to month in the degree of positiveness of serum of untreated syphilitic patients varied slightly.

Fordyce, Swift, Craig and others have for many years taught that the negative Wassermann reaction during or after treatment is of no convincing value of cure unless it remains negative for at least two years, with no development of symptoms, no suggestion of positiveness in the reaction frequently repeated during the period of observation, and of course the negative and assuring clinical, neurologic, and serobiologic examination of the nervous system and the spinal fluid. With the first of these as a criterion, it appears that mercury salicylate alone and in the doses given has shown little evidence, from my own short period of observation on this series, or the longer period of observation of Nelson and Anderson, as qualifying as a curative agent in latent syphilis.

Should a similar opportunity present itself again, I shall give mercury salicylate intramuscularly in increasing doses from 2 to 2½ grains each week, if the patients give no evidence of mercurialism.

SUMMARY

Eighty-seven previously untreated latent syphilitic patients with 4 plus Wassermann reactions were given 1 grain of mercury salicylate intramuscularly at weekly intervals for courses of from six to eight injections. The Wassermann reaction immediately after treatment remained strongly positive in 66 per cent. of the cases. In only 9 per cent. was there a reversal to negative; and in some such patients who were given a third Wassermann test after an interval without treatment, the reaction was positive. It seems fair to conclude with Nelson and Anderson, who carried on a similar study in 1915, that mercury salicylate alone in the dosage and for the period given does not qualify as a curative agent in syphilis. The plans for a longer study were curtailed by the demobilization. In the future, mercury salicylate will be used in increasing doses up to 2 and 2½ grains weekly in an effort to learn whether mercury salicylate in larger doses is effective.

I acknowledge the aid given in this study by Dr. Rivera of San German, of Pharmacist Valera of Ponce, and of the Drs. Guiterez and Gonzales Martinez of San Juan, Porto Rico.

15 Central Park West.

# FOLLICULITIS DECALVANS AND LICHEN SPINULOSUS

## A CLINICAL COMBINATION *

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The depilating folliculitides compose a complex and little understood group of dermatoses, as is indicated by the variety of names given to these conditions by different authors. The terms folliculitis decalvans and pseudopelade, with which we are most familiar, usually call to mind processes producing baldness of the scalp alone. The literature shows, however, that a clinical picture similar to that of folliculitis decalvans may be seen on other hairy parts of the body, either in association with the disease on the scalp, or independently. Pringle,[1] Robinson [2] and others have described cases in which folliculitis decalvans of the scalp has been associated with a similar pathologic process in other parts. Among those who have described a similar picture in hairy parts other than the scalp, and without any accompanying involvement of the scalp, are Mewborn,[3] Darier,[4] and Arnozan,[5] the latter, under the title "Depilating Folliculitis of the Limbs," describing a condition which he said he would have likened to pseudopelade if it had occurred on the scalp. Lastly, we are familiar with lupoid sycocis of Milton or ulerythema sycosiforme of Unna,[6] and ulerythema ophryogenes of Taenzer and Unna,[7] two conditions which have much in common with folliculitis decalvans.

This paper is not concerned, however, with folliculitis decalvans associated with similar lesions elsewhere, but rather with the combination of folliculitis decalvans on the scalp, and lichen spinulosus on the body. Attention was first given to this combination when Graham Little [8] presented a case before the Dermatological Section of the Royal Society of Medicine in 1915, and it is interesting to note that the only other two cases on record were seen in Great Britain

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* Read before the Section on Dermatology at the Seventy-First Annual Session of the American Medical Association, New Orleans, April, 1920.

1. Pringle: Brit. J. Dermat. **7**:117, 1895.
2. Robinson: Jour. Cutan. & Gen.-Urin. Dis. **23**:268, 1905.
3. Mewborn: Jour. Cutan. & Gen.-Urin. Dis. **22**:589, 1904.
4. Darier: Ann. de dermat. et syph. **32**:58, 1901.
5. Arnozan: Ann. de dermat. et syph. **23**:491, 1892.
6. Unna: Monatsh. f. prakt. Dermat. **9**:134, 1889.
7. Taenzer: Monatsh. f. prakt. Dermat. **9**:197, 1889.
8. Little: Brit. J. Dermat. **27**:183, 1915.

in the same year, the second one being presented before the same society by Dore,[9] while the third one was described in detail by Wallace Beatty[10] of Dublin.

## REPORT OF CASES

Case 1.—*History.*—Little's patient was a woman, 55 years of age, sent to him by Dr. Lassueur of Laussane, who wrote "The aspect of the skin seems to me to recall lichen spinulosus, especially the lesions of the flexual folds and the armpits. But the condition of the scalp is very unusual, and I am altogether embarrassed to make a diagnosis which fits in with the skin affection." The condition had begun ten years before, when the patient developed an inflammatory condition of the vertex of the scalp which resulted in a slow shedding of the hair and the development of bald patches. Subjective symptoms were lacking, and the trouble was ignored. Five months before Little saw the patient a similar, although much more rapid, inflammation accompanied by great itching, became apparent on the side and front of the scalp, and the hair came out in handfuls; at the same time an itchy eruption was manifest in the axillae, groins and the flexures of the elbows. In these positions there was a folliculitis in grouped patches with a general resemblance to lichen spinulosus, while on the back and on the exterior surfaces of the upper arms there was a diffuse, slightly spiny folliculitis, also itchy and reddened. The hair of the scalp, axillae and groin had been almost entirely destroyed, but the atrophy apparent in the scalp was not yet present in the axillae and groin. Little said that the condition on the scalp was obviously familiar under the name of folliculitis decalvans. He had thought of Darier's disease, but the distinct alopecia and the exclusive follicular location of the lesions in the case excluded that diagnosis.

*Discussion of Case.*—In the discussion which followed the case presentation, all of the speakers — Pringle, Morris, Adamson, Sequeira and MacLeod — agreed that the condition on the scalp was folliculitis decalvans, but there was a considerable difference of opinion as to the nature of the eruption on the body, some of the speakers considering it a possible early form of Darier's disease, while others were convinced that it was not. In a later discussion, however, Little asserted definitely that it was a true lichen spinulosus.

Case 2.—*History.*—Dore's[9] patient was also a woman, aged 43. The case bore a rather close resemblance to that of Little's. A typical folliculitus decalvans had been present for two years. Nine weeks before she was shown she developed a follicular eruption indistinguishable from lichen spinulosus on the abdomen, back, chest, thighs, neck and ears. This eruption consisted chiefly of minute, scattered, skin-colored, acuminate or spiny noninflammatory papules; a few were larger, and reddened or excoriated.

*Discussion of Case.*—In discussing this case, Little stated that the body lesions in his case were more definitely spiny than those in Dore's, and that he considered the spiny eruption in Dore's case a coincident lichen scrofulosorum, while Adamson felt that all that could be said about the condition on the body was that it was a folliculitis.

Case 3.—*History.*—Beatty's[10] case was carefully investigated and reported in detail. The patient, a woman of 43 years, had an eruption on the scalp and upper part of the body, presenting a combination of cutaneous symptoms unlike any combination which he had seen previously. He said only the scalp sug-

9. Dore: Brit. J. Dermat. **27**:295, 1915.
10. Beatty: Brit. J. Dermat. **27**:331, 1915.

gested folliculitis decalvans; the condition on the body resembled lichen spinulosus as occasionally seen in children, though of a coarser kind. The hair had begun to fall ten years previously, coming out in patches, gradually, without soreness, until after some years an almost universal baldness was produced. Itching of the head was at times troublesome. The eruption on the body began a month before Beatty saw the patient, appearing as a "roughness of the skin." The upper part of the chest anteriorly was first affected, but the condition spread and similar roughness appeared on the scalp.

*Examination.*—This revealed a scalp of cicatricial aspect, smooth and bald, throughout the greater part. Here and there were small, hard islets of follicular prominences, and formed by an accumulation of dry, horny material, some of them were pierced by short hairs. These groups of follicular plugs developed in association with the eruption on the body. On the neck, body and limbs were groups of follicular elevations, some with prominent horny spines such as are seen in lichen spinulosus of children. This eruption was widespread, but there were few lesions on the lower portion of the trunk. They were all follicular, there was a universal tendency to grouping, and the color varied from flesh color to reddish brown. The spines in the smaller lesions were fine and hairlike, and blunt in the larger lesions. They could be picked out intact, leaving a gaping folliculiar opening.

In his remarks, Beatty states that he was struck by the resemblance of his case to that of Graham Little's, a history of shedding of the hair dating back some years, followed by an acute condition like lichen spinulosus on the body. Little's and Dore's cases and his own had led him to believe that the combination of these two conditions, which he had at first regarded as merely accidental, constituted a clinical unity. He proposed calling this combination of atrophic baldness of the scalp and lichen spinulosus "Lassueur's and Graham Little's syndrome." Tissue examination in this case showed the "corps rond" described in Darier's disease, the "psorosperms" being few and discovered only after the study of a large number of sections. As Webber says, if these bodies are to be considered pathognomonic of this disease, then his case must be regarded as an atypical Darier's disease.

CASE 4.—*History.*—My patient was a woman, aged 30, seen in Dr. W. A. Pusey's practice, in October, 1919. The disease began when she was 9 years of age. At that time her hair began to fall rather rapidly, the alopecia being permanent. This alopecia has been slowly progressive since that time. Eight years ago she developed an eruption over the back which she says was similar to the present attack, but it cleared up spontaneously. The present exacerbation began four or five months before the patient was seen. The first lesions appeared over the nape of the neck, followed by others over the occipital region, shoulders and back. This condition was complicated in September, when a number of boils appeared over the scalp and back. The hair had been shed rapidly again after this eruption appeared on the body. The patient's personal history disclosed nothing of interest. Her general health had always been good, and she had never had any serious illness. She suffered from chronic constipation, but had used laxatives regularly and had a daily bowel movement. Menstruation was regular and normal. The Wassermann reaction was negative.

*Examination.*—This disclosed two clinical pictures. The scalp showed an extensive alopecia, most of the hair having disappeared, while the remaining hair was found in patches, as shown in the photograph. The skin of the bald areas showed an extreme atrophic scarring of the type seen in folliculitis decalvans. The process which had produced this atrophy was still active,

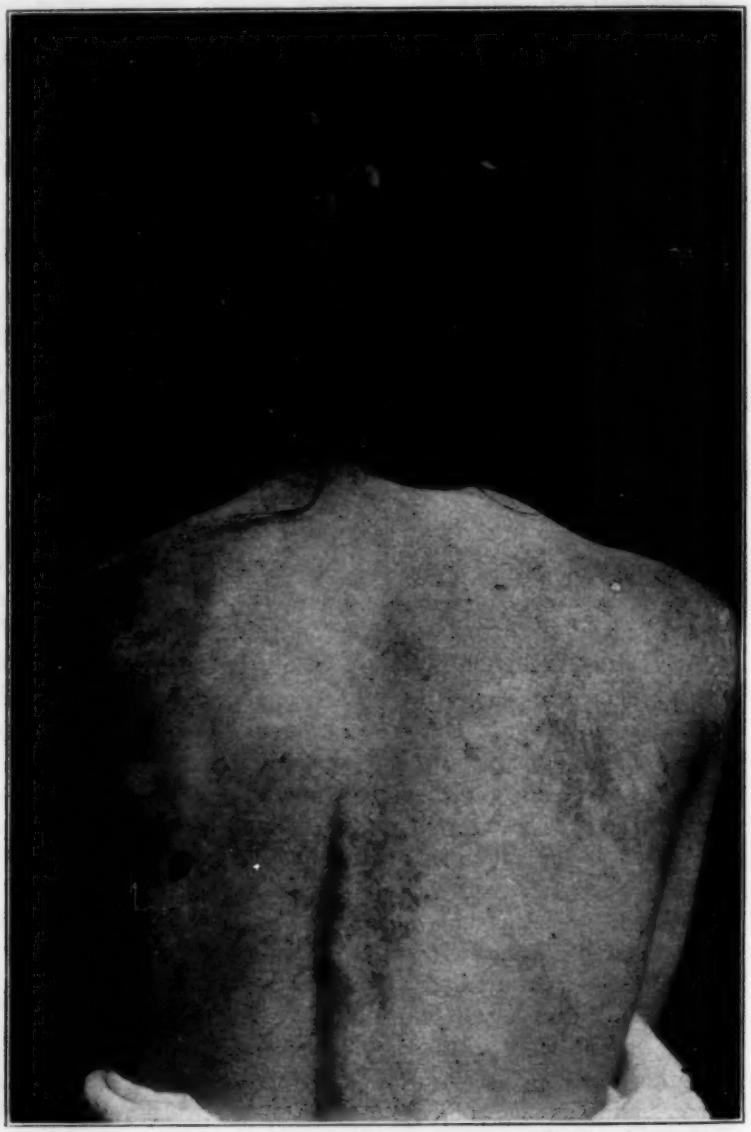
numerous follicular papules and a few pustules being present. The other eruption, involving the nape of the neck, lower occipital region, shoulders, back and upper arms, consisted of variously sized groups of follicular lesions. The individual lesions varied from reddish follicular papules, slightly elevated, to definitely elevated and spinous lesions, some of them having rather long, slender spines. In the largest patches the lesions had slightly inflammatory areolae, so that the group picture showed an erythematous background with elevated follicular lesions. In the smaller groups the erythematous background was lacking, showing it to be secondary. Removal of one of the spinous lesions left a dilated follicular orifice. The lesions varied from a grayish to a reddish color, while the group was dull red. The patient, who was refractory, refused biopsy, and passed from observation before any therapeutic attempts could be made.

## SUMMARY AND COMMENT

All of these four cases occurred in women, aged, respectively, 55, 43, 43 and 30 years. In all, folliculitis decalvans was of long standing (ten, two, ten and twenty-one years, respectively), followed by the rather sudden development of a follicular eruption of the body whose clinical picture was that of lichen spinulosus. In all cases the condition on the scalp was obviously folliculitis decalvans, but the body eruption was more puzzling. In the discussion of Little's case, an early Darier's disease was considered, but Little had been able to rule this out to his own satisfaction, and in a later discussion stated definitely that the condition was lichen spinulosus. Dore considered the eruption in his case to be clinically indistinguishable from lichen spinulosus, as did Beatty in his case, although it will be recalled that the histologic picture suggestive of Darier's disease was disturbing. In my case no suspicion of Darier's disease could be entertained. The exclusive follicular location of the papules, the distribution of the eruption, the extreme alopecia, the lack of a greasy seborrheic element, the grouping and the spinous character of the lesions readily eliminate that disease. I am convinced that this combination is not to be regarded as merely an unusual keratosis follicularis.

No attempt has been made to explain the association of these two conditions, and this is not surprising when we consider that we are dealing with two conditions, each of obscure etiology. Coincidence would scarcely serve as an explanation, since each of them is an uncommon disorder. It is difficult to consider the eruption on the body as folliculitis decalvans, since in none of the four cases was there any atrophic scarring in the body lesions, as is the case when folliculitis decalvans affects parts other than the scalp. Furthermore, the body eruption was too acute.

I wish to suggest, however, one hypothesis which is founded on a comparative basis. We are familiar with other follicular eruptions, which are looked on as manifestations of the activity of toxins secreted



Alopecia and eruption over back, neck and shoulders in Case 4.

by infectious organisms affecting distant parts of the body. The most familiar example of this kind is the lichen scrofulosorum type of tuberculid. More recently we have become acquainted with the group of trichophytids, first described by Jadassohn in 1911, consisting for the most part of lichenoid eruptions occurring on the body of children affected with trichophytosis capitis, usually kerion celsi. In a number of these cases the eruption assumed a type clinically indistinguishable from lichen spinulosus, as shown by Jadassohn,[11] Bloch,[12] Guth,[13] Rasch [14] and others.

In the condition under consideration we have some points in common with the above conception of the etiology of lichen scrofulosorum and lichenoid trichophytids; folliculitis decalvans being almost certainly due to a chronic infective process, which, theoretically at least, might be able to elaborate toxins responsible for the production of lichen spinulosus. In support of this view may be offered the opinion of Adamson,[15] who is probably best acquainted with lichen spinulosus; he suggests that a toxic etiology is the most plausible one for the condition. Furthermore, in at least two of the cases (Beatty's and my own), the process on the scalp, as evidenced by the alopecia, had become more active at the time of appearance of the lichen scrofulosorum; and we know that in the case of the tuberculids, the eruption often appears at a time when the tuberculous process has been lighted up by some factor, as in the case of lichen scrofulosorum following measles. The above hypothesis is offered, it should be understood, only as a suggestion, for I had no opportunity to study the patient with this view in mind.

In conclusion, I should like to say that this paper was offered to call attention to this combination of clinical conditions in the hope that recognition and study of other cases might result in a better understanding of its significance.

## ABSTRACT OF DISCUSSION

Dr. J. M. King, Nashville, Tenn.: I had a patient who had lichen spinulosus, but I do not recall that she had any disturbance of the hair or folliculitis. The hair growth was poor and thin; she complained of itching but had no scalp involvement. The diagnosis in this case was confirmed by Dr. George MacKee and Dr. Howard King.

Dr. F. W. Cregor, Indianapolis: We do not have as much folliculitis decalvans in this country as in Europe. I recall seeing many boys in the

11. Jadassohn: Autoreferat i, Cor.-Bl. f. schweiz. Aerzte, **42**:24, 1912.
12. Blocki: Die Allgemein-pathologische Bedeutung der Dermatomykosen, Halle, p. 82, 1913.
13. Guth: Arch. f. Dermat. u. Syph. **118**:856, 1914.
14. Rasch: Brit. J. Dermat. **28**:9, 1916.
15. Adamson: Brit. J. Dermat. **17**:39, 1905.

clinics there begging to be relieved of the scars following this disease that they might emigrate to America. I have not observed lichen spinulosus in any cases of folliculitis decalvans. I have observed, however, lichen spinulosus following lichen ruber planus in two patients, both of whom had received arsenic for more than 120 days. I think that arsenical medication had something to do with the process in Dr. Senear's case.

Dr. Walter J. Highman, New York: I had a patient with what I thought was pityriasis rubra pilaris on the body and patches on the head of what seemed to be alopecia areata but which proved to be pityriasis rubra pilaris.

Dr. Oliver S. Ormsby, Chicago: In November, 1919, I presented a patient before the Chicago Dermatological Society with a condition which was practically identical with that reported by Dr. Senear. It was presented as an example of folliculitis decalvans and lichen spinulosus. I think five cases are now on record. The patients all had a similar history and probably represent a disease group which has not heretofore been reported.

Dr. Francis E. Senear, Chicago: Dr. Ormsby's case and mine corresponded in nearly every detail in the clinical picture, except that the scalp involvement in my case was more extensive than in Dr. Ormsby's case. Arsenic might well furnish a basis for the development of lichen spinulosus. In the English literature there is not infrequent reference to the development of spinous lesions in lichen planus, similar in character to those of lichen spinulosus. It is possible that Dr. Cregor has seen that type of lichen planus, but it does not seem probable that the treatment he mentioned would have cleared up the cases so readily and permanently had they been true lichen planus lesions.

# THE ASSOCIATION OF HERPES ZOSTER AND VARICELLA*

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The possibilities of this subject are obviously extensive, but space limitations will not permit more than an occasional reference to the etiology, epidemiology and immunology of zoster and varicella. I shall attempt to do two things: first, to report a case of associated herpes zoster and varicella which in some of its relations is almost unique in medical literature; and second, to present certain recommendations deduced from an examination of the literature on this particular association which, if followed, would contribute to the clarification of a subject upon which there is now great confusion.

The report presented covers a case which falls into Group 3 in the classification given below: A man with zoster developed varicella which he passed on to a daughter not otherwise exposed.

## REPORT OF A CASE

*History.*—The patient, a physician on the house-staff of a sanatorium, in early middle life, of regular habits, in good general health and with a negative medical history, presented two sets of skin lesions involving the face, the trunk, arms and legs, and the mucous membrane of the tongue. Those on the left side of the face appeared first, being preceded for about twenty-four hours by a burning pain in the left temple of such nature and severity as to suggest the possibility of an accidental contact of the part with an acid. The lesions consisted of numerous groups of vesicles, situated on a more or less diffusely reddened integument, and containing serous material; at several places the contents were hemorrhagic. By the third day the local pain was marked; there was considerable general malaise with moderate temperature; the anterior auricular and the upper anterior cervical glands became enlarged and painful; the vesicles increased in number, some appearing on the tongue; an edema of the lids closed the left eye. The condition was obviously a rather severe zoster involving the upper and middle branch of the fifth cranial nerve. Five days after the inception of the attack, at the time when the zoster was at its height, there appeared on the other parts of the face and scalp, and on the trunk, arms and legs, lesions quite evenly distributed, forty to fifty in number, consisting of macules, slightly pruritic but not painful and quite intensely erythematous, from the center of which vesicles emerged, becoming pustular in about twenty-four hours. Some of these were umbilicated, but hemorrhagic lesions were not present. The second eruption was recognized as varicella, and the patient was placed in the usual quarantine. The zoster lesions cleared up in about twelve days, leaving a few depressed scars; the varicella disappeared after about the same length of time, leaving no trace.

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Ten days after the beginning of the varicella lesions, the patient's 3-year-old daughter, who had been in contact with him before and during the quarantine, became ill with typical varicella. In the father's case there was no known exposure to chickenpox, and no knowledge of his ever having had that disease. The daughter had been exposed to the condition only through the father. As to focal infection as a cause of the zoster, there were no obvious foci to be found, but an exhaustive examination of the teeth and tonsils to determine the presence of infective material was not made.

### CASES REPORTED IN LITERATURE DIVIDED INTO FOUR GROUPS

The number of cases of associated herpes zoster and varicella reported in the literature was placed by LeFeuvre [1] in January, 1915, at forty. Four years later, Low [2] states that over fifty have been recorded. I have been able to find somewhat less than fifty, and as a number of references were not available, the correct number is probably in the neighborhood of sixty.

For the purposes of brief review, these cases may be grouped into four classes:

1. Herpes zoster in one patient followed by varicella in others who were exposed.

2. Herpes zoster in one patient followed by varicella in the same patient not followed by varicella in others who were exposed.

3. Herpes zoster in one patient followed by varicella in the same patient followed by varicella in others who were exposed.

4. Varicella in one patient followed by herpes zoster in others who were exposed.

GROUP 1.—Fully two-thirds (about forty) of all reported zoster-varicella cases belong to Group 1.[3] If frequency of occurrence of cases in this group may be estimated from the number of reports of cases suddenly made in England in 1913, when in the period from May to December sixteen cases were recorded in the literature, it seems probable that since 1888, when Bokay first called attention to

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1. LeFeuvre: Brit. M. J. **1**:15 (Jan. 2) 1915.

2. Low: Brit. M. J. **1**:91 (Jan. 25) 1919.

3. Walker: Brit. M. J. **1**:1192 (May 31) 1913. Bruce: ibid. **1**:1194 (May 24) 1913, and **2**:584 (Aug. 30) 1913. Cressy: ibid. **2**:528 (Aug. 23) 1913. Roberts: ibid. **2**:584 (Aug. 30) 1913. Harrison: ibid. **2**:712 (Sept. 13) 1913. Oakes: ibid. **2**:712 (Sept. 13) 1913. Coates: ibid. **2**:712 (Sept. 13) 1913. Willson: ibid. **2**:712 (Sept. 13) 1913. Milne: ibid. **2**:896 (Oct. 4) 1913. Orr: ibid. **2**:1048 (Oct. 18) 1913. Busfeld: ibid. **2**:1124 (Oct. 25) 1913. Bartlett: ibid. **2**:1340 (Nov. 15) 1913. Quinn: ibid. **2**:574 (Nov. 23) 1918. Hepworth: ibid. **2**:529 (Oct. 10) 1914. Destinn: ibid. **1**:633 (April 10) 1915. Low: ibid. **1**: (Jan. 25) 1919. Heim: Berl. klin. Wchnschr. **49**:2349 (Dec. 2) 1912. Richardson: Lancet **2**:1732 (Dec. 13) 1913. Fordyce: Edinburgh M. J. **23**:34 (July) 1919. Bokay: Wiener klin. Wchnschr. **22**:1323, 1909.

the association of the two conditions, a large number of Group 1 cases have occurred that have not been reported.

An average case of this group develops thus: The patient has an attack of zoster; in about fourteen days varicella is found in some one exposed to the zoster patient without discoverable exposure to varicella elsewhere. While these reported cases are free from serious doubt as to the correctness of the zoster and varicella diagnoses, it must be admitted that for the determination of less obvious things many are incomplete in clinical description. Such significant items as the age of the zoster patient and the location and severity of the zoster attack are not infrequently omitted. The time interval preceding the appearance of the varicella is practically always given as this seems to be accepted as an important factor in the diagnosis. In forty-eight cases of varicella originating from thirty-two cases of zoster the average interval was fourteen and one-sixth days, the extremes being two and twenty-one days. In a large number of cases the diagnosis "varicella" or "chickenpox" is given directly without description of the number and nature of the component lesions. The question of exposure of the varicella victim to other possible sources of infection is almost always considered, but in few cases is a previous varicella in the zoster patient discussed.

In explanation of these cases Bokay,[3] who himself reported nine instances of the association, advances the theory that under certain unknown conditions the infective agent of varicella produces a local zosteriform eruption instead of a generalized exanthem; the zoster is thus an expression of varicella, and contagion is readily passed to others. He quotes Henoch,[4] Thomas,[5] Jennings[6] and Swoboda,[7] in support of the theory, and proposes the term "zoster varicellosa" to designate the condition. Other advocates of the theory are LeFeuvre,[8] who suggests a clinical term of similar import to Bokay's, namely, "varicella herpetica"; and Heim,[3] in whose report the varicella lesions (in a boy: source, zoster in mother) were zoniform in the right axilla, this area being also the seat of zoster-like pain.

GROUP 2.—This group, in which zoster in one patient is followed by varicella in the same patient, but not by varicella in others exposed, is particularly interesting in that it brings into consideration the entire subject of so-called generalized herpes zoster. In fact, it is impossible to discuss this group without including the latter condition. Under

4. Henoch: Vorlesungen über Kinderkrankheiten, Ed. 6. Berlin, 1892.

5. Thomas: In Ziemann's Handbuch der spec. Pathologie und Therapie, Vol. 2.

6. Jennings: In Keatings Encyclopedia of Diseases of Children **1**:761.

7. Swoboda: In Pfaundler-Schlozmann: Handbuch der Kinderkrankheiten, **1**:732.

various captions such as "Herpes and Varicella," "Herpes Zoster with Aberrant Vesicles," "Herpes Zoster and Chickenpox," "Association of Zoster and Chickenpox," and "Varicella Accompanying Herpes Zoster," a scant dozen cases assignable to this group have been reported by Orr,[8] Williams,[9] Ffrench,[10] Frances and Goldberg,[11] Downes,[12] Corlett[13] and Head.[14] Some of these reports are also lacking in clinical detail, and the diagnosis of varicella does not always seem to be free from some element of doubt. In Orr's case the varicella appeared three days after the onset of the zoster and was "typical in character and distribution." In Williams' case the zoster lesions merely "looked like chickenpox," and as there appears to have been no general distribution, the case should be excluded from Group 2. In the case reported by Ffrench the interval was one day, and the only description of the generalized eruption given was the word "crop"; the diagnosis of "chickenpox complicated by herpes zoster" was made by a health officer, but Ffrench, himself, considered it a case of zoster with aberrant vesicles. In two of the cases reported by Frances and Goldberg the second eruption was "varicelliform," appearing two and three days after the onset of the zoster; in the third a varicella is described, but a time interval is not mentioned. In Downes' case the rash which appeared seven days after the beginning of the zoster was "indistinguishable from varicella," but it should be added that the patient had taken phenacetin and morphin for the zoster pain, and that several in the family who had not had chickenpox, including a new-born babe, escaped that condition, though no attempt was made at isolation. In Corlett's reported cases, the first showed lesions "strikingly like varicella in appearance and distribution" with a five-day interval preceding; the diagnosis of varicella was concurred in by an eminent colleague; the second, with a six days' interval, showed a vesicular eruption which was simply diagnosed "varicella." The notes on the third case are scant, but the eruption corresponded to those of Cases 1 and 2; the fourth, after an interval of several days, showed an eruption which conformed to that of varicella. Three of these cases were in adults past middle life. Corlett apparently did not associate the two conditions etiologically, and while recognizing the rarity of the coincidence, was apparently more impressed with the unusualness of varicella occurring in adults,

8. LeFeuvre: In Guy's Hosp. Gaz. **32**:101, 1918.
9. Williams: Brit. M. J. **2**:584 (Aug. 30) 1913.
10. Ffrench: Brit. M. J. **1**:388 (Feb. 11) 1899.
11. Frances and Goldberg: J. A. M. A. **70**:1061 (Apr. 13) 1918.
12. Downes: Brit. M. J. **1**:307, 1919.
13. Corlett: J. Cutan. Dis. **23**:289 (July) 1905.
14. Head: Allbutt's System of Medicine, Ed. 1, **8**:630.

for he adds, without giving detailed reports, that he had seen two cases suggestive of the combination in children. (This attitude of mind toward varicella in adults was found several times in the literature usually also exerting an influence on diagnosis.) Head's patient, after a one-day interval, showed "typical chickenpox spots."

In this group of eleven cases the time interval between the two eruptions in eight instances was from one to seven days, the average being three and one-half days. It should be noted that this is much less than the average time interval given for Group 1, which was fourteen and one-sixth days. In ten, the description of the second eruption corresponds to that of varicella; in one, only the word "crop" is used; in ten, the distribution includes enough of the body surface to warrant the designation "generalized." Although the second rash was in all instances diagnosed as varicella, it is extremely significant that no case of chickenpox is recorded as having developed from exposure to combined zoster and varicella. This is so contrary to what would be expected that one may with propriety question whether in every instance the diagnosis of varicella was correct. If not varicella, these cases would fall into the category of so-called generalized herpes zoster.

This term, generalized herpes zoster, is used rather loosely in the literature. It is impossible to say exactly how many cases have been recorded. Not including the reports of bilateral zoster,[15] and without considering the literature of the etiology of zoster, I have been able to find at least twenty-six cases;[16] the number is much larger if cases mentioned but not reported in detail are included. In these reports three descriptive terms are used, namely: herpes zoster with aberrant vesicles, generalized herpes zoster and universal herpes zoster. The first two terms are employed rather indiscriminately, but the last is fairly self-explanatory. A better and more inclusive designation as a substitute for this term would be "multiple herpes zoster," meaning

15. For an excellent bibliography of bilateral herpes zoster, see Stelwagon's Diseases of the Skin, Ed. 7, Philadelphia, W. B. Saunders Company.

16. Pernet: Brit. J. Dermat. **26**:399, 1914. Schamberg, J. F.: Generalized Herpes, J. A. M. A. **54**:532 (Feb. 12) 1910. Arkwright: Quoted in London Lancet **2**:1223, 1900. Fasal: Arch. f. Derm. u. Syph. **95**:27, 1909. Haslund: Nordisk. Med. Archiv., Vol. 8, 1897; and Kaposi's Festschrift, 1900. Weidenfeld: Arch. f. Derm. u. Syph. **96**:87, 1909. Uhlmann: ibid. Ehrmann: ibid. Lipschultz: ibid., quoted in Steuer's article (see below). Mackay: Glasgow M. J. **48**:278, 1897. Janselme and Leredde: In Lancet **2**:822, 1898. Tenneson: Traité de Dermatologie, Paris, 1893. Girandeau: Bull. de la Soc. d. hôp., Seance du July 29, 1898, quoted by Fasal. Steuer: Wiener klin. Wchnschr. **61**:1167, 1911. Molinié: These de Paris, No. 97, 1895-96. Beyer: Arch. f. Derm. u. Syph. **78**:233, 1913. Tryb: Dermatologische Wchnschr. **59**:983, 1914. Fischl: Arch. f. Derm. u. Syph. **118**:553, 1913. Nobl: Wiener klin. Wchnschr. **24**:14, 1911. Parkes Weber: Internat. Clin., Ser. 26, **3**:185, 1916.

the disturbance of more than one group — possibly all groups — of posterior root ganglions producing multiple areas of massed zoster lesions. This would include the rare instances of bilateral zoster and the oft-quoted case of universal zoster by Columbini pictured in Mracek's Handbuch.[17] But the expressions "aberrant vesicles" and "generalized" zoster need to be more clearly defined. Tenneson,[16] who originated the term "aberrant vesicles," says that they are few, isolated, look like those of the zoster group, are distributed irregularly at great distances from each other over the entire body, developing slowly, disappearing perhaps without being noticed, and occurring in nine out of ten cases. Crocker and Mracek confirm this stated frequency of occurrence. Molinié [16] says that extensive zoster always, and moderate zoster usually, shows these vesicles, and that they do not become necrotic. Unfortunately, cases fitting Tenneson's description have repeatedly been termed "generalized herpes zoster." It is, therefore, impossible at the present time to state exactly what is meant by the two terms. Fasal [16] suggests that the term "aberrant vesicles" be limited to lesions in the neighborhood of the zoster area, and that the term "herpes zoster with generalized eruption" be applied to the more extensive and intensive outbursts, thus avoiding the implication that the second rash is necessarily a zoster.

It is obvious that the "aberrant vesicles" and "generalized zoster" types may closely simulate varicella, and it is especially interesting that the rash in the generalized cases is practically always described in terms which link it with the idea of varicella. Some of these expressions are: "suspected of being smallpox but looked like chickenpox;" "like varicella;" "varicella-like spots;" "varicelliform." This similarity to varicella is apparent when the clinical details are examined more fully. Vesicles were present in fourteen cases; vesicles with opaque contents were observed in seven; with hemorrhagic contents in four; umbilicated, two; in the mouth, two; like those of chickenpox, four, and grouped, three. Papules were also present in seven. Lesions appeared in successive crops in seven; areola was present in five. The number of lesions ranged from thirty to several hundred distributed practically over all parts of the body. As to time interval, in five there was none; in two, one day; in three, from four to seven days; in four no mention of time was made; the average time interval was one and seven-tenths days. Thus it is seen that this group of "generalized" zoster is strikingly like Group 2 of our classification in which varicella was the diagnosis given for the second eruption. A significant difference is found in the time interval between eruptions: namely, one and seven-tenths and three and five tenths days. Otherwise the similarity is

17. Mracek's Handbuch der Hautkrankheiten **1**:692.

so great that one questions whether the difference is not in some instances one of terms only. A varicella erroneously called a "generalized zoster" remains a varicella and vice versa.

GROUP 3.—This group of our zoster-varicella classifications combines the clinical element of Groups 1 and 2; that is, the patient with zoster not only develops varicella himself, but passes it on to others. As mentioned above, about fifty cases in the first two groups have been reported; instances, however, which fit the requirements of Group 3 seem to be of extreme rarity. The case herewith reported is one; the generalized eruption which showed itself five days after the appearance of the zoster in a man who had never had varicella, was clinically in every detail a typical varicella, and the child who, following exposure to this zoster patient, developed varicella after a ten day's incubation period, was known positively not to have been exposed to that disease elsewhere. In the literature, up to the present, I have been able to find only two cases which might by liberal interpretation be placed in this group; neither of them is a clear-cut case. In one case reported by Grey,[18] two varicellas developed after exposure to a case of right thoracic zoster, with one or two lesions on the left chest; the diagnosis of chickenpox was made after recovery and was based on the fact that these spots outside the zoster area left "scars like those of varicella." The second case is reported by Weber:[16] A man with leukemia under treatment with arsenic developed a typical zoster about the right shoulder, five days later a generalized but scanty eruption of varicella-like lesions appeared over the body; a boy exposed to this patient left the hospital and in ten days became ill with varicella. Weber says: "It is worth mentioning, but it is doubtless a mere coincidence."

GROUP 4.—This group is a logical outgrowth of the preceding groups: If zoster can lead to varicella, why should not varicella lead to zoster? Four cases have been found recorded by Dando,[19] Aikman,[20] and an anomynous observer.[21] Dando reports attending a man with zoster whose son had had chickenpox four weeks before; some years before in the same family he had cared for the mother who had had a zoster which appeared five weeks after a varicella in a daughter. In Aikman's report a boy returned to a boarding school with an unhealed varicella; seven days later his teacher, who had never had varicella developed a right thoracic zoster; varicella appeared also in other

18. Grey: Brit. M. J. **1**:377 (Mar. 29) 1919.

19. Dando: Brit. M. J. **2**:1340 (Nov. 15) 1913.

20. Aikman: Quoted by Parkes Weber; from LeFeuvre: M. J. of South Africa **9**:77, 1914.

21. Guy's Hospital Gazette **27**:219, 1913.

children. The anonymous observer reports that a boy of 13 showed a zoster two and one-half weeks after exposure to chickenpox. These cases are lacking in clinical detail and prove little or nothing; they are, however, extremely suggestive of important possibilities.

## COMMENTS

From the foregoing consideration of the literature it is evident that, while an etiologic relationship in certain cases of herpes zoster and varicella must be accepted, much needs to be done toward the clarification of confused points. There is an urgent call for more careful and more complete clinical observation. Some of the items which should receive closer attention from clinicians are:

Since every patient with zoster has varicella as a possible causative factor and vice versa, inquiry should always be made of a zoster patient regarding possible exposure to and a previous attack of varicella; and every varicella patient should be questioned as to possible exposure to a zoster victim and as to previous zoster attacks.

To check up on the theory of Bokay, Heim and others, every varicella case should be examined with special reference to a possible grouped or zonaform distribution of lesions and to a history of neuralgic pain in such lesions. Incidentally, adult years must not be given undue weight in excluding a varicella.

In order to establish the correctness of the statements of Tenneson, Crocker and others as to the frequency of the so-called "aberrant vesicles," every zoster patient should be examined daily, if possible, for the presence of lesions outside the zoster area. If aberrant vesicles are found or if more extensively distributed lesions appear, in order to determine the nature of the second eruption and to establish a sound basis for differential diagnosis, a complete observation should be made concerning time relationship of the two eruptions; possible influence of drugs used in treatment; the condition of the zoster lesions when the general lesions appeared; number of the latter and positional relation to the zoster area; type or types of lesions in the general eruption; the symptom of pain; appearance in crops and observation as to whether the lesions are hemorrhagic, umbilicated, necrotic or surrounded by an areola. Every detail that might be of value in differentiating the zoster vesicle from the varicella vesicle should be searched for and noted.

Finally, as an essential step in clearing away the haze which envelops the present conception of "generalized herpes zoster," that term should be abandoned as indefinite and inaccurate and a new nomenclature established. This group should be rearranged under the captions given above, namely: (*a*) Herpes zoster with aberrant vesi-

cles, restricting the lesions to the neighborhood of the zoster area as suggested by Fasal instead of the wider distribution of the original definition; (*b*) herpes zoster attended with a general eruption, and (*c*) multiple herpes zoster, to include bilateral and universal cases.[22]

## ABSTRACT OF DISCUSSION

DR. OLIVER S. ORMSBY, Chicago: About ten years ago I saw a patient who presented a typical and marked case of herpes zoster of the face and scalp, and on the fourth day of the zoster a generalized varicella-like eruption developed. I have never satisfied myself as to what this might be, but it belongs in one of the groups described by Dr. McEwen.

DR. EVERETT S. LAIN, Oklahoma City: A group of diseases of which herpes zoster is one, no doubt has its etiology based on some toxic product of bacterial nature. It can now be easily understood from the reports that have been made, why varicella, variola and other diseases may possibly have herpes zoster associated with them.

DR. GEORGE P. LINGENFELTER, Denver: A few months ago I saw a case of undoubted herpes zoster associated with marked neuralgic pain. This patient had been exposed to smallpox some days before. Five days later he developed typical smallpox.

DR. J. M. KING, Nashville, Tenn.: In pneumonia, concurrent with the infection, herpes simplex develops in 33 per cent. of cases, due, no doubt, to the pneumococcus. Why could there not be an organism in varicella which has a predilection for nerve tissue, thus producing herpes zoster? Both varicella and herpes zoster produce immunity. Why could not the organism of varicella produce herpes zoster just as the pneumococcus produces herpes simplex?

DR. WALTER J. HIGHMAN, New York: Herpes is a disease *sui generis* and has no connection with herpes zoster. The pathology is similar. True herpes zoster has no connection with any other disease. The zoster may be due to the same micro-organism that causes the varicella; in other words, they may be different clinical expressions of the same agency. but the zoster-like eruptions are not true zoster. The latter never recurs.

DR. RICHARD L. SUTTON, Kansas City, Mo.: I thought herpes zoster was usually due to infection or to injury of one of the posterior ganglions. I did not know that it was a disease *sui generis*.

DR. ERNEST L. MCEWEN, Chicago: I made no attempt to discuss etiology for I found the subject so broad that I could not do so in the time allowed. I am convinced that herpes zoster may have a number of infective causes.

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22. The following references were not available:
LeFeuvre: M. J. of South Africa **12**:77, 1914; ibid. **13**:133, 1918.
Minet and LeClerque: Clinique **6**:100, 1911.
Janselme and Touraine: Bull. de la Soc. francais. de Derm. et syph. **25**:351 (July 2) 1914.
Janselme and Leredde: Bull. et mém. Soc. méd. de hôp. de Paris. **15**:619, 1898.
Watson: Guy's Hosp. Gaz. **29**:186 (Apr. 24) 1915.
Wainwright: ibid. **27**, May 10, 1913.
Heatherby: ibid. **28**, April 25, 1914.

It is possible that the organism of varicella and also of smallpox is capable, under certain conditions, of producing the clinical picture of zoster. The real purpose of this paper was to emphasize the following: first, that these cases are occurring much more frequently than the literature indicates; second, that the reports in the literature are incomplete and insufficient; third, that it is imperative that clinicians and pathologists should examine most thoroughly these cases of zoster combined with other eruptions in order to find out everything possible about them; fourth, the desirability of abandoning the term "generalized herpes zoster," and substituting for it the three terms given, as covering more accurately all the types observed. It is only by more careful and complete observation that we will arrive at a more accurate knowledge of the association of herpes zoster and varicella.

# A FEW EARLY NOTES ON SYPHILIS IN THE ENGLISH COLONIES OF NORTH AMERICA

JOHN E. LANE, M.D.
NEW HAVEN, CONN.

"It is only from the most scanty materials that we can trace the origin and progressive improvements in the healing art among the early settlers of the American colonies," and American medical literature was an almost unknown product before the beginning of the Revolution. In the earliest days there were few physicians in the Colonies, and in New England "the practice of medicine was in many instances united with the parochial duties of ministers of religion, who by their amiable manners, zealous attention and pious converse, endeared themselves to their people." [1]

The population was too small to attract many physicians, and skilful men of the profession "were of rare occurrence in the colony. They seldom, it would appear, partook of the religious zeal that brought other emigrants across the Atlantic. Dr. Robert Child was one of the earliest physicians to come to New England, though he never practiced medicine there. For a long time he has been given the reputation of being "an advocate of general religious toleration and freedom of conscience," but Kittredge has recently shown that "he abhorred these principles with all the strength of his earnest soul as the devil's latest device for the ruin of society and the damnation of mankind." Instead of toleration and freedom, he, an ardent Presbyterian, was "eager to extend to all his countrymen the blessings of a rigid conformity, . . . . and to subvert the Massachusetts government, to bring the Colony under the thumb of a Presbyterian Parliament, to impose the Solemn League and Covenant upon all its inhabitants, and to procure the establishment of the (Presbyterian) Church of England as a state church." [2]

There is little reference to venereal disease in the colonial literature of the period, and in New England such diseases were undoubtedly rare because of the "stern morality" of the people and because of the severe punishment meted out to those who were discovered in sexual irregularities.

It is also probable that the few who suffered from such afflictions would postpone as long as possible the disclosure of their disease to the physician who was also their pastor, and whose "pious converse"

1. Thatcher, James: American Medical Biography **1**:14, 1828.
2. Kittredge, G. L.: Doctor Robert Child the Remonstrant. Reprinted from the Publications of the Colonial Society of Massachusetts, Cambridge **21**:1919.

might be especially unwelcome at such a time. And what would be the plight of an erring youth when, as in the case of John Wilson of Medfield, the pastor, schoolmaster and physician was one and the same person? This good physician was the son of the minister of Boston, of the same name, of whom it was said that he was a man "than whom orthodoxy in New England had no champion more cruel and ungenerous, and whose zeal and passion led him to revile and even strike prisoners being led away from the judgment seat," and who vociferated in his pulpit that "he would carry fire in one hand and faggotts in the other to burn all the Quakers in the world." [3]

### FIRST KNOWN OUTBREAK OF SYPHILIS IN NEW ENGLAND

The first known outbreak of syphilis in New England occurred in 1646, and is described at length in the "Diary of John Winthrop." Though it has often been quoted, it is curious enough to bear an occasional repetition. Preceding the description by a few pages, is the following entry:

> October, 1645. At Ipswich there was a calf brought forth with one head, and three mouths, three noses and six eyes. What these prodigies portended the Lord only knows, and in his due time he will manifest.[4]

The writer does not state that the omen referred to the outbreak of syphilis, but that is the first calamity recorded in his diary.

> There fell out also a loathsome disease at Boston, which raised a scandal upon the town and country, though without just cause. One of the town ——— having gone cooper in a ship into ———, at his return his wife was infected with lues venerea,[5] which appeared thus: Being delivered of a child, and nothing then appearing, but the midwife, a skilful woman, finding her body as sound as any other, after her delivery, she had a sore breast, whereupon divers neighbors resorting to her, some of them drew her breast, and others suffered their children to draw her, and others let her child suck them (no such disease being suspected by any), by occasion whereof about sixteen persons, men, women and children, were infected, whereby it came at length to be discovered by such in the town as had skill in physick and surgery, but there was not any in the country who had been practised in that cure. But

3. Adams, Brooks: The Emancipation of Massachusetts, 1887, p. 135.

4. Winthrop, John: The History of New England from 1630 to 1649, edited by James Savage, Boston **1**:254, 1826.

5. Savage, the editor, adds the following in a footnote: "The first two blanks in this paragraph were once filled, the first probably with the person's name, the second with that of the place, but they have been effectually erased. In such an important narrative it may be of little consequence that it was first written, the man "infected his wife, and leaving her with child went to sea again; the woman knew all, but not what she ailed. So that reports were various. Whether the result, as stated in the text, be the truth or not it is of less consequence than to observe, how the ignorance of our fathers on this topick gives confirmation to the general opinion of their blameless manners."

(see the good providence of God) at that very season there came by accident a young surgeon out of the West Indies, who had had experience of the right way of the cure of the disease. He took them in hand, and through the Lord's blessing recovered them all ——— in a short time. And it was observed that although many did eat and drink and lodge in bed with those who were infected and had sores, etc., yet none took it of them, but by copulation or sucking. It was very doubtful how the disease came at first. The magistrates examined the husband and wife, but could find no dishonesty in either, nor probable occasion how they should take it by any other (and the husband was found to be free of it). So it was concluded by some that the woman was infected by the mixture of so many spirits of men and women as drew her breast (for so it began). But this is a question to be decided by physicians.[6]

It seems probable that Dr. Child made use of this outbreak of syphilis in his Remonstrance, which was made about the same time, for in it is found the statement that the "hand of our good God . . . seems to be against us. . . . Yea at this time laying his just hand upon our familyes, taking away many to Himself, striking others with unwonted malignant sickness, and some with shameful diseases."[7]

### TREATMENT OF SYPHILIS IN COLONIES

The search for remedies for syphilis among the plants of the New World began almost with its discovery. Guaiac was the most celebrated drug found there. Its virtues were widely heralded, and Fracastor sung of it as follows: The place on

which the Spanish navigators were the first to land . . . they called Hispaniola (Hayti). This land is sown with gold; but that which makes a greater wealth for it than gold is the precious tree to which the natives of the country have given the name of Guaiac. . . . And Diana, O Prodigy, has not completed her career when the action of the remedy is already revealed. The pustules dry, the ulcers heal, the pains disappear, and the flower of youth is born again with the return of health.

Many herbs and roots were tried in early Colonial days for syphilis as well as for other diseases. Some were shown to the colonists by the Indians, and native medicines were a necessity, the distance from England and the isolation of the small settlements making a sure supply of medicines impossible. One or two examples of the treatment used for syphilis may be of interest.

A popular medical book, which ran through several editions about 1730, entitled "Every Man His Own Doctor or The Poor Planter's Physician. Prescribing Plain and Easy Means for Persons to Cure

6. Winthrop, John: The History of New England from 1630 to 1649, edited by James Savage, Boston **1**:257, 1826.

7. Hutchinson Papers, Albany, p. 215.

Themselves of All, or Most of the Distempers, Incident to This Climate, and with very Little Charge, the Medicines Being Chiefly of the Growth and Production of This Country," gives the following description of syphilis and its treatment, which is the same as that prescribed for yaws:

> The Pox may be cured exactly in the same Manner: And because the Symptoms are much the same, it is very probable, the one was a Graft of the other (i. e., Yaws). The pious *Spaniards* catch'd it from their *Negro* Mistresses in the *West-Indies,* and had the Honour of propagating it from thence to all the rest of the World.
>
> In both cases, confine yourself altogether from eating Flesh, from a strong Drink, and be very careful of catching Cold.
>
> To avoid these Misfortunes, eat seldom of fresh Pork which breeds very gross Humours; live not too near a Swamp; not ever venture upon strange Women, especially upon Ethiopians.

So much for etiology and prophylaxis. The treatment is described as follows:

> Take 1 Ounce of the Bark of *Sumac Root,* 1 Ounce of the *inner Bark of Pine,* and 2 Ounces of the Bark of *Spanish Oak;* boil these together in 2 Quarts of *Water* 'til the *Decoction* be very strong. Of this Liquor drink a full Pint, Milk-Warm, and immediately after it, Half a Pint, quite cold: and it will give you a powerful Vomit.
>
> The next Morning, take Half a Pint of the same *Drink* warm, and the same Quantity again in the Evening; and continue to doing, for 6 Weeks, or 2 Months; only the *Vomit* must be repeated every seventh Day. In the mean Time, gargle your Throat, and wash all your Sores and Ulcers with the same warm Liquor, which ought to be made fresh every 2 Days. Beside all this, you must chew the *Sumac* Root very often, and swallow the healing juice.
>
> Every Night, before you go to Rest, take 2 *Pills,* made of *Turpentine* and *Deers Dung* in equal Quantities.[8]

Another treatment is of special interest because it was introduced by John Bartram, the botanist. Bartram, who with Benjamin Franklin, was one of the founders of the American Philosophical Society, was not a physician, but he had a penchant for medical matters "and he even acquired so much knowledge of the latter science, as to be very useful: and in many instances he gave great relief to his poor neighbors, who were unable to apply for medicines and assistance to the physicians of the city" (Philadelphia).[9]

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8. Everyman His Own Doctor or The Poor Planter's Physician, Ed. 2, Williamsburg and Annapolis, William Parks, 1734, p. 50. (A third edition was printed in the same year by B. Franklin. The book has been attributed to John Tennant.)

9. Darlington, William: Memorials of John Bartram and Humphrey Marshall, 1849, p. 38.

Lobelia is the plant he described for use in syphilis. This description is found in a pamphlet published as an appendix to Short's Medicina Brittanica, an American edition of which was edited by Bartram, and published in Philadelphia in 1751 by B. Franklin and D. Hall Few copies of the pamphlet are now to be found. It is entitled: "Mr. Bartram's Appendix: containing *Descriptions, Virtues* and *Uses* of sundry Plants of These Northern Parts of *America;* and Particularly of the Newly Discovered *Indian* Cure for the *Venereal Disease.*" The book contains this description:

*Lobelia.* This curious Plant riseth from a fibrous Root to three or four Feet high, with a Spike of Blue Flowers surrounding the Stalk for near a Foot in Length: It grows in rich shady Ground; it is a scarce Plant in many Parts of the Country.

The learned *Peter Kalm* (who gained the Knowledge of it from Colonel *Johnson,* who learned it from the *Indians,* who, after great Rewards bestowed on several of them, revealed the Secret to him) saith, That the Roots of this Plant cureth the *Pox* much more perfectly and easily than any mercurial preparations, and is generally used by the *Canada Indians,* for the Cure of themselves, and the *French* that trade amongst them, tho' deeply infected with it. They take a Handful of the Roots, and boil them in a Quart of Water, and drink the Decoction, beginning with Half a Pint at first, if the Patient be weak, then increase the Dose every Day as he can bear its purging; but if he can't bear it every Day, let him omit it a Day or two, then take to it again, as he finds Occasion, until he is cured: They wash the Ulcer with the Decoction; but if it be deep and rotten, they put some Powder of the inner Bark of the Spruce-tree into it, which helps to dry it up, but if the Disease is inveterate, they drink the Decoction of *Ranunculus Folio Reniformis.* An old *Sachem* told Colonel *Johnson* of another Shrub, with a red Root, from which proceeds several slender Branches, eighteen Inches or two Feet long, on which grow Spikes of white Flowers, which produce three-square black Seed-Pods; the leaves some of our People drink as Tea, and some smoak it with Tobacco; the Roots of this, bruised and boiled, and the Decoction drank, the *Sachem* said, he rather preferred to the *Lobelia;* but the *Lobelia* seems to be of the most general Use, and with extraordinary Success.

*More particular Directions how to use the Lobelia-Root for the Venereal Disorder, obtained from the Indians, by Col. J.*

"After making a Decoction of it, the Patient is to drink about two Gills of it very early in the Morning, fasting, the same before Dinner, and Bedtime. Add or diminish as you find it agree with the Patient's Condition: The third Day begin Bathing, and continue it twice a Day, until the Sores are well cleansed, and partly healed, then use the Lotion but once a Day till quite well; observing all the Time to use a slender Diet (vegetable Food, and small Drink) as in other Courses of Physick, a Salivation excepted. These are the Directions I have had from the Person who gave me the Secret."[10]

10. Short, Thomas: Medicina Brittanica, Ed. 3, Reprinted, Philadelphia, 1751, B. Franklin and D. Hall. Appendix by John Bartram. Mr. Bartram's Appendix: containing descriptions, virtues and uses of sundry plants of these northern parts of America; and particularly of the newly discovered Indian Cure for the Venereal Disease, p. 5.

# News and Comment

## A NEW JOURNAL OF DERMATOLOGY

"Ceska' Dermatologie" is the name of a new journal recently founded in Prague. The first number appeared October, 1919, and is dedicated to Professor Janowsky. The managing editors are Prof. F. Samberger and Priv. Doz. Dr. A. Tryb. The journal is issued in the Czeck language, is a monthly, and is devoted to dermatology and venereal diseases.

# Abstracts from Current Literature

## EXPERIMENTAL STUDIES ON THE INVESTIGATION OF THE NATURE OF THE ANAPHYLACTOID CONDITION CAUSED BY THE REPEATED INTRAVENOUS INJECTION OF ARSPHENAMIN. Norimasa Hirano, Kitasato Arch. Int. Med. **2**: (April) 1919.

After discussing the symptoms and various theories concerning the causation of this dreaded reaction, Hirano mentions Milan's work which he thinks gives a clue to the cause. In this work is mentioned that the previous administration of epinephrin has successfully prevented the development of an anaphylactoid condition in a patient who used to manifest the phenomenon. Hirano also mentions the fact that the development of this condition was successfully prevented by administering a dose of arsphenamin in two portions, a smaller portion to be injected one hour before the larger portion. From these facts the author was led to believe that there may exist some intimate relation between arsphenamin and the suprarenal systems in the development of the anaphylactoid state.

To this end Hirano made several experiments on rabbits: 1. An experiment to ascertain the change of the chromaffin substances in the suprarenal glands caused by the injection of arsphenamin.

Various quantities of arsaminol and neo-arsaminol were injected into healthy rabbits. The dose ranged from 0.007 to 0.7 gm. per kilo body weight. After various intervals the rabbits were killed or bled to death. The suprarenal glands were then extirpated and the chromaffin reaction was determined. It was found that if a large amount of arsphenamin was injected (0.8-0.07 per gram kilo weight), the chromaffin reaction was very weak one hour after the injection; but if a small quantity, for example, a therapeutic dose was used, the reaction was produced in a widely differing intensity which was sometimes difficult to distinguish from that exhibited in the control.

2. An experiment to ascertain epinephrin contents of the bilateral suprarenal glands after injection of arsphenamin and neo-arsphenamin.

For this experiment, the epinephrin content of the bilateral suprarenal glands of normal rabbits was first determined, and was found to be on the average 0.2 gm. Five rabbits then received injections of arsphenamin in large quantities, 0.06-0.07 gm. per kilo weight. They were killed one hour after the injection. There was a remarkable decrease of the epinephrin contents in these rabbits, the average being 0,116 gm. Hirano then determined the influence of arsphenamin on the epinephrin contents, when arsphenamin was injected in therapeutic amounts. He wished to determine whether the epinephrin contents decreased in quantity and if so, how long it took before the normal content was regained.

More than ten rabbits were injected with from 0.001 to 0.03 gm. of arsphenamin per kilo weight. The animals were killed from one to four hours after the injection, and it was found that the epinephrin contents diminished in amount, not only in therapeutic dose. They even were decreased by so small a quantity as from 0.002-0.003 gm. per kilogram. By the injection of smaller doses, such as 0.001 gm. per kilogram weight, no decrease was effected. With reference to the decrease of the epinephrin contents and the final return to

normal, after an injection of arsphenamin, Hirano found that the decrease reached its minimum in six hours from the time of injection of a large quantity of arsphenamin, i. e., 0.06 gm. per kilogram. It then gradually regained its former state. The recovery was nearly complete in from ten to twenty-four hours and complete in forty-eight hours.

With reference to neo-arsphenamin, Hirano found that the epinephrin content of both suprarenals decreased but that the amount was normal in two hours. The maximum therapeutic dose of neo-arsphenamin did not produce any decrease in the epinephrin contents of the suprarenals.

3. Investigation of the Causes of the Decrease of the Epinephrin Contents of the Bilateral Suprarenal Glands after the Intravenous Injection of Arsenic Compounds: These tests were carried out after the Trendelenburg's method and after what the author calls the frog perfusion test.

A rabbit was injected with 7 c.c. of a 1:200 arsphenamin solution or 0.02 gm. per kilogram body weight. Blood was withdrawn just before, immediately after and one hour after the intravenous injection of arsphenamin. The serum prepared from blood withdrawn immediately after an injection of arsphenamin did not produce as remarkable a change in the number of drops as did the serum taken before the injection of arsphenamin. The serum, one hour after the arsphenamin injection, also produced a similar result as the one immediately after the injection. From this Hirano concludes that the epinephrin contents of the serum immediately after and one hour after the injection of arsphenamin were less than those of normal blood. The experiment was repeated in different rabbits and the serum to be tested was taken before, immediately after, two hours, and two and a half hours after the injection of arsphenamin. The experiment showed that the number of drops will decrease by the perfusion of untreated serum, but that it will return to the former state in about thirty minutes. The change produced by the perfusion of the serum that is prepared from blood withdrawn immediately after injection will be repaired in the course of eighteen minutes. The decrease in the number of drops that was produced by the perfusion of the serum taken immediately after the injection of arsphenamin was not so great as the one obtained with untreated serum. The decrease of the number of drops by the perfusion of the serum that was prepared from blood withdrawn after two and a half hours was most remarkable. The change was noted in the course of more than one hour after the perfusion.

Hirano concludes from these experiments that "a remarkable decrease in the number of drops resulted from the perfusion of the serum prepared with the blood of an animal that had not yet received any intravenous injection of arsenic compounds, or the normal serum. By perfusion of the serum treated with arsenic a far less remarkable decrease was, however, produced, and the repair of the change in the drop-frequency, moreover, was seen to take place sooner. This decrease of the drop frequency was far more remarkable by the perfusion test made with the serum that had been prepared after from 2 to 2½ hours from the intravenous administration of arsenic, than was the case with normal serum. Thus it will be seen that the epinephrin-like substance contained in the blood serum is diminished in quantity immediately after the intravenous infusion of 0.02 gm. per kilogram body weight of arsphenamin, but that it increases after the lapse of two or two and a half hours after the injection. Another series of tests made with 0.03 gm. of arsphenamin per kilogram body weight brought about nearly the same results. The change in the number of drops by perfusion test made with the blood plasma was not so manifest as with blood serum.

The increase or decrease of the vasocontractile substance in blood serum does not prove the increase or decrease of the epinephrin contents of the circulating blood from which the serum has been prepared. But, considering the fact that arsenics have been proved to interrupt the epinephrin-sublimate reaction in vitro, the introduction of arsenics into the circulating blood by means of intravenous injection may play a part in the decrease of epinephrin in the same blood.

The increase of the epinephrin-like substance that is brought about after a lapse of two or two and a half hours after intravenous injection of arsenic compounds may partly be interpreted by the assumption that the decrease of epinephrin in the circulating blood may result in the invigoration of the function of the suprarenal systems, and especially of the suprarenal glands, in order to compensate the deficiency of the blood constituents. The change in the quantity of epinephrin-like substance in blood serum, however, may not be fully explained by this assumption, because we are as yet left in ignorance regarding the nature and the function of the epinephrin-like substance found in the circulating blood. It may be conjectured, however, that this substance would be produced from some preexisting mother substance in the blood by coagulation, and that this preexisting mother substance must have been destroyed by arsenic compounds introduced into the circulating blood, but that afterward it must have been increased by compensatory production from the suprarenal systems.

Hirano concludes from the above experiments that the decrease of the epinephrin contents of the suprarenal glands may be explained by the assumption that some part of the arsenic compounds introduced into the circulating blood may find its way to the suprarenal glands and there combine with the epinephrin, while the remaining part may lead to the immediate decrease of epinephrin in the circulating blood, which process may excite the splanchnic nerve and cause an invigorated secretion of epinephrin from the suprarenal glands in order to compensate the deficit in the blood.

Hirano then conducted experiments to determine the changes that take place in the suprarenal glands after repeated intravenous injections of arsphenamin or neo-arsphenamin, and found that the epinephrin contents of the suprarenal glands of rabbits after three intravenous injections of 0.02 gm. per kilogram weight, given once a week, were sometimes increased. Even when a therapeutic dose of arsphenamin is given to the animal thus treated, no remarkable decrease of the epinephrin contents of the suprarenal glands is observable. On the contrary, when a rabbit is given an intravenous injection of 0.03 gm. per kilo body weight for three weeks, the epinephrin contents of the suprarenal glands are the same as those of normal rabbits. But if a therapeutic dose of neo-arsphenamin is given to an animal thus treated, a remarkable decrease of the epinephrin contents of the suprarenal glands is observed.

GUTIERREZ, Manila.

UEBER DIE VANADIUMTHERAPIE BEI SYPHILIS (CONCERNING VANADIUM THERAPY IN SYPHILIS). FERDINAND WINKLER, Dermat. Wchnschr. **70**:147 (March 6) 1920.

"If one injects a cubic centimeter of a 2 per cent. solution of sodium vanadate into a primary lesion of syphilis in such a manner that a part of the fluid infiltrates the sclerotic tissue and a part infiltrates a zone surrounding the entire lesion, a characteristic retrogression of the syphilitic granuloma

is to be noted as early as the next day; the indurated wall or border becomes smaller and the characteristic color of the efflorescence wanes; smear preparations show only disintegrated particles of spirochetes and the dark-field examination is negative.

"Should this local injection be repeated during the following three to four days, the sclerosed part heals, skin forms over the lesion and the induration of the tissue disappears.

"Likewise the results with broad condyloma when similarly treated locally are those of apparent healing. There is a corresponding repair of the syphilitic tissue and a disappearance of the spirochetes from the tissue juices. This healing, however, is more gradual, and more local injections are necessary than with the above lesions."

If one injects sodium vanadate into a syphilitic inguinal gland, the response in many cases is a swelling followed by a rapid healing. Frequently, however, there is a resorption of the gland proliferation without the intervening swelling. Whereas, before the sodium vanadate injection the gland will yield on aspiration material rich in spirochetes, soon after the injection the aspirated material shows great diminution in the number of spirochetes.

"In rebellious cases of indurative edema, vanadium injection into the edematous tissue frequently brings about rapid improvement. Moreover, local vanadium therapy favorably influences the syphilitic lymph channels.

"Sclerotic rests, such as one not seldom sees for some time after the outbreak of exanthemas, rapidly diminish under the influence of local vanadium injections. Disintegrating gummas face about under this treatment, the necrotic mass disappears, leaving a well-healed scar. Fissures of the folds of the mouth also quickly heal."

Scaling syphilids of palms and soles react favorably under this local treatment. Macular forms, on the other hand, are not appreciably influenced by vanadium therapy. Leukoplakia of the mouth mucous membrane shows no appreciable improvement with vanadium therapy.

"The basis of vanadium therapy in syphilis depends on the great toxicity of vanadium for the spirochetes."

This action of vanadium on spirochetes and trypanosomes has been proved experimentally in great detail by Proescher and Seil (*Am. J. Syphilis* **1**: No. 2 [April] 1917).

This toxic action in all probability depends on the high oxidation properties of vanadium salts, especially in conditions where vanadinic acid ($HVO_3$) is an intermediate product.

The pharmacologic and the toxicologic action of various vanadium salts is discussed. The work of various authors is cited. Vanadium pentoxid and ammonium metavanadate are the most toxic of the salts of vanadium which have been tested. Sodium hexavanadate and vanadyl sulphate, on the other hand, are the least toxic. The salts of pyrovanadinic acid are less toxic than those of orthovanadinic acid, and the latter in turn are less toxic than those of metavanadinic acid.

Toxicity is manifested in animals by circulatory disturbances, failing respiration, disturbance of the heat regulation center and coma. There may be albuminuria, cylindruria and finally anuria. There is increased intestinal peristalsis and bloody diarrhea and congestion of the lung and portal vessels.

In man the intravenous injection of sodium tetravanadate (in quantity corresponding to 20 mg. ($V_2O_5$) has resulted in lacrimation, depression of the pulse, incontinence of feces, irregular frequent respiration and a lowering of

the temperature 3 C. Other symptoms that have appeared are dry bloody cough, loss of appetite, anemia and nervous disturbances. Postmortem sections show definite and widespread pathologic change. The toxic dose of sodium tetravanadate in man (according to Proescher and Seil) corresponds to about 20 mg. of $V_2O_5$ when injected intravenously. This quantity is well tolerated when injected subcutaneously or intramuscularly.

Helouis and Delarue have employed small doses of vanadium salts as a stimulus of the appetite and to improve the general condition in tuberculosis. Various other French authors have reported favorably on the use of various vanadium salts as alteratives. The body, however, quickly acquires a tolerance and frequent periods of rest from the drug is advised. Vanadium has been used in anemia, chlorosis, tuberculosis, diabetes, neurasthenia, acute and chronic rheumatism and in various nutritional disturbances.

As a germicidal agent vanadium salts have no value. Streptococci, meningococci and the bacilli of diphtheria, tetanus, edema, typhus, dysentery and enteritis withstand from 0.2 per cent. to 0.8 per cent. solutions from two to eight days. Tubercle bacilli were still viable after being in a 5 per cent. solution of sodium tetravanadate for four weeks. *Trypanosoma Brucei,* in contrast to *Trypanosoma equiperdum,* are soon destroyed by vanadium salts.

Experimentally with guinea-pig syphilis, vanadium salts seem to possess a specific action against spirochetes. In experimental lesions of the testicles the spirochetes are quickly destroyed and the lesions heal.

The experimental work of A. W. Stillians (Chicago) is commented on. Stillians reports the largest series of cases (thirty-two) in which vanadium therapy has been tested. The syphilitic lesions soon disappeared in each case and the dark-field examinations speedily became negative. Stillians reports, however, that in none of the cases treated exclusively by vanadium therapy did the Wassermann reaction become negative.

The author advocates vanadium therapy in early syphilis and as an adjunct to arsphenamin therapy.

ELBERT CLARK, Chicago

EXPERIMENTAL SYPHILIS IN THE RABBIT. I. PRIMARY INFECTION IN THE TESTICLE. WADE H. BROWN and LOUISE PEARCE, J. Exper. Med. **31**:475 (April) 1920.

Using two strains of *Spirochaeta pallida,* all rabbits used were infected after an incubation period of from two to six weeks.

The testicular reactions were of two fundamental types: one in which the reaction was intense with acute exudation and infiltration to be followed by subsequent recurrences; the other types being more chronic and consisting largely of infiltration and proliferation. A third group tended to combine the characteristics of both of the others. The duration of the testicular process varied from four weeks to six months, being, in general, inversely proportional to the intensity of the local reaction.

EXPERIMENTAL SYPHILIS IN THE RABBIT. II. PRIMARY INFECTION IN THE SCROTUM. PART I. REACTION TO INFECTION. WADE H. BROWN and LOUISE PEARCE, J. Exper. Med. **31**:709 (June) 1920.

Animals with thin and delicate scrotal skin were selected for this work, the inoculation being made by implanting a small piece of infected testicle or granulomatous skin nodule in a pouch prepared in the scrotum. The specific reaction is the same by all methods of scrotal inoculation. In the use

of a virus emulsion the incubation period varied from one to four weeks, the initial reaction in the scrotum appearing in one of three general forms: (1) small circumscribed swellings or diffusely spreading patches of a rose-pink color situated in the papillary and reticular layers of the skin, being gelatinous in character and frequently associated with a rich vascular network; (2) a minute, translucent nodule or indurated plaque in the papillary layer more superficial than the first, and (3) an opaque, porcelain-white nodule of extreme hardness in the depths of the scrotum. The first two were the most frequent and earliest.

The development of the chancres was marked by an extension of the reaction, spreading diffusely through the scrotum. The various types are described in detail.

The incubation period for tissue implants and virus inoculation was much the same although the reaction following implants must be regarded as partly wound healing, partly foreign body reaction and partly specific. The later development of the chancres was influenced by various degrees of edema, congestion, irregularities in granulation process and acute inflammatory reaction.

PART 2. SCROTAL LESIONS AND THE CHARACTER OF THE SCROTAL INFECTION, p. 729.

Typical scrotal chancres are divided into nodular and lenticular or discoid varieties, depending on the part of the scrotum in which they develop and also on the mode and rate of development. The nodular type was also divided into two groups—one with moderate necrosis and ulceration, the other with slight ulceration or none.

The course of the infection appeared to be about the same as it is when the testicle is infected, although subject to great variations individually. The scrotal lesions disappeared spontaneously after a period varying from a few weeks to months.

EXPERIMENTAL SYPHILIS IN THE RABBIT. III. LOCAL DISSEMINATION, LOCAL RECURRENCE AND INVOLVEMENT OF REGIONAL LYMPHATICS. WADE H. BROWN and LOUISE PEARCE, J. Exper. Med. **31**: 749 (June) 1920.

Three general types of local reaction were recognized in this work: (1) a diffuse reaction with the formation of multiple foci of secondary reaction arising subsequent to the development of the primary lesion; (2) a reaction characterized by the formation of lesions having a perivascular arrangement, and (3) dissemination of the infection with the production of multiple lesions showing no demonstrable connection with the primary focus of infection.

Recurrent lesions were identical in all respects, whether the primary lesion had healed spontaneously or had been assisted by artificial means.

A regional adenopathy always follows the initial lesion although there may be no lesions to indicate this dissemination. An examination of the inguinal glands shows, however, that they are involved shortly after inoculation and that a pallidum reaction may be detected there before a scrotal infection is recognized.

JAMIESON, Detroit.

PARAPLEGIA AFTER ARSPHENAMIN. T. J. DIMITRY, J. A. M. A. **74**:1150 (April 24) 1920.

Dimitry reports an interesting case of a man who suffered a complete loss of sight before any other symptoms developed to make possible a diagnosis, though some precursory symptoms obtained in his history were not recognized

at the time as being important. Fundus examination elicited a distinct elevation of the optic nerve of both eyes. This elevation was greater in the right eye. The pupils were widely dilated and did not respond to light. Tests for syphilis were negative. Following the intravenous injection of 0.06 gm. of arsphenamin, the patient complained of stiffness in the legs and pain in the back. He could not move his right leg and during the afternoon this paralysis extended to the other leg. It was necessary to catheterize the bladder and later to contend with an overflow of the urine. He suffered an inability to evacuate the bowels, and subsequently an incontinence of feces. He developed decubitus and a painful hyperesthetic area of the left arm. The paralysis of the legs was absolute, and all voluntary motion and sensation in all its qualities, including temperature and touch, was destroyed. Varying degrees of deep and superficial anesthesia and hyperesthesia extended to within an inch of the nipple anteriorly, and not quite so high posteriorly. The reflexes were abolished in the legs with a flaccid paralysis and the appearance of a rapid wasting. Two days after the injection of arsphenamin, the elevation in the optic nerve had improved and within the next day had disappeared entirely, leaving a normal appearing optic nerve, though the patient was blind. In spite of the apparently harmful effect of the arsphenamin, a second dose of 0.06 gm. of arsphenamin was given, and a dose of 0.09 gm. of neo-arsphenamin was given a few days afterward. Mercury was used by inunctions and the iodids were used in increasing doses, and for weeks the patient received 75 drops of saturated solution of potassium iodid three times a day. Seven months later the patient could walk and had practically perfect vision. There remained some bladder disturbance. Though the Wassermann test was negative both for the blood and for the spinal fluid, the other tests showed that the etiology was that of syphilis. Dimitry urges that it is well to remember that syphilis presents a vagary of symptoms at times, lacking a definite explanation. What appears as an incongruous syndrome both pathologically and clinically is often made clear when syphilis is taken into consideration and an appreciation of the changes that might occur from a syphilitic arteritis, better known as a Huebner arteritis.

WAUGH, Chicago.

FURTHER EXPERIENCE WITH SODIUM GYNOCARPATE (SODIUM GYNOCARDATE "A") AND A TRIAL OF SODIUM MORRHUATE IN LEPROSY. SIR LEONARD ROGERS. WITH NOTES OF CASES BY JOGESPH CHANDRA MUKERJEE, Indian M. Gaz. **54**:165 (May) 1919.

Rogers believes that the more effective higher melting point preparations consist chiefly of hydnocarpic (melting point 59-61) and chaulmoogric (melting point 68) acids with sufficient of the lower melting point preparations to make the salts soluble in water. Basing his belief on the results of his experiments, Rogers found the sodium salt of hydnocarpic acid most active in leprosy. He treated a series of cases with a preparation made of Hydnocarpus wightiana oil, consisting mainly of sodium hydnocarpate with sufficient of the lower melting-point acids to make it soluble, and also containing a little sodium chaulmoograte. The melting point of the mixture of fatty acids is approximately 48 C., and Rogers found the products obtained from cheaper and more easily obtainable hydnocarpus oil at least as efficient in leprosy as that obtained from true chaulmoogra oil.

Rogers treated fourteen cases with this mixture. The disease was present in different forms, tubercular and mixed types. The duration of the disease

was from six months to fifteen years with an average duration of 3.4 years. The dose given ranged from 0.5 c.c. to 5 c.c. of a 3 per cent. solution. The duration of the treatment is from six months to fourteen and one-half months, the average duration being eight and one-tenth months. The results obtained were: slightly improved, 1; much improved, 6; lesions disappeared, 7.

Rogers reviews also the cases treated with sodium gynocardate (hydnocarpate) reported in the *Indian Journal of Medical Research,* vol. 5, October, 1917, and reports the present condition. Of fourteen patients who were not lost sight of or died of intercurrent diseases, five have remained well for over a year, and two more for shorter periods; two advanced cases remain greatly improved and one slightly improved; one showed no improvement and three have had relapses. All of the patients were in an advanced state, and Rogers thinks that the results obtained are highly encouraging.

Febrile Reactions after Sodium Hydnocarpate: Rogers believes that milder reactions are beneficial to the patient. Microscopic examinations have shown that the softening and shrinking of tubercular lesions of leprosy under the influence of sodium hydnocarpate intravenously is regularly accompanied by breaking up of the lepra bacilli until either only a minute red spot remains, or they disappear. This may occur without any febrile or local reactions being observed, but more rapidly when mild reactions take place. The fever, Rogers believes, is due as in the case of tuberculosis, to the liberations of toxins consequent to the breaking up of the organisms. The fever may be so great and prolonged as to temporarily break down the resisting power of the patient, and even cause the spread of the disease for a time. This is specially true in greatly thickened tissues so that especial caution is necessary in increasing the dosage.

Rogers cannot predict a complete cure and complete eradication of the lepra bacilli from the system on account of the relapses reported, but he thinks the results already obtained are sufficiently encouraging to stimulate further work along these lines.

*Part II. Sodium Morrhuate in Leprosy.*—This is prepared from cod liver oil, and is found to have the great advantage over sodium hydnocarpate of producing little pain or induration on subcutaneous injections. Sodium morrhuate can also be injected intravenously and is far less irritating to the veins than sodium hydnocarpate. Although Rogers cannot draw definite conclusions, owing to the short time that the drug has been used, he believes it to be a very active drug in the treatment of leprosy.

He concludes with this important observation: "that the breaking up and eventual disappearance of the bacilli and good progress in leprosy under sodium morrhuate show that there is nothing absolutely specific against leprosy in chaulmoogra oil products, so other unsaturated fatty acids may also be expected to yield effective preparations against acid-fast bacilli of both leprosy and tuberculosis. Nor is such action, as far as we yet know, limited to the resistant acid fast bacilli, and thus a vast field of research is opened up."

GUTIERREZ, Manila.

GRANULOMA INGUINALE. DOUGLAS SYMMERS and ALBERT D. FROST. J. A. M. A. **74**:1304 (May 8) 1920.

The authors have recently had occasion to study two chronic ulcerative lesions of the groin occurring in negroes. Since in the tropics, there are many granulomatous formations about which little is known, it is impossible at

present to state with certainty whether the various chronic ulcerative lesions occurring in the region of the groin and external genitals are manifestations of one and the same process or anatomically related reactions arising in response to different causative agents, or the result of combined factors. However this may be, there is at least one variety of granuloma inguinale that has been frequently observed and whose clinical features appear to be much the same, no matter in what country they are seen. In this particular variety, cell inclusions were described by Donovan in 1905 and have since been found in ulcerative lesions of the groin in widely remote parts of the world. These intracellular inclusions have been studied by Walker, who regards them as small encapsulated bacilli belonging to the Friedländer group. The evidence that they bear a causative relationship to granuloma inguinale, however, appears not to have been definitely established. On the other hand, it has been suggested that the presence of these intracellular bodies is due to secondary infection of venereal or other pudendal lesions and that, once established in the tissues, they dominate the local pathologic process and promote destruction of tissue. In the secretions in both the cases reported, intracellular bodies morphologically identical with those described by Donovan were found. One of the cases appeared to represent a typical example of granuloma inguinale as encountered in various parts of the tropics. The other, however, was possibly syphilitic in nature.

WAUGH, Chicago.

## SUPPLEMENTARY REPORT ON THE TREATMENT OF LEPERS WITH GYNOCARDATE OF SODA "A." E. MUIR, Indian M. Gaz. **54**:130 (April) 1919.

This report is supplementary to a report on the treatment of thirty lepers which appeared in the June, 1918, number of the *Indian Medical Gazette*. Muir reports in detail the thirty cases previously reported, and compares the action of sodium gynocardate and sodium morrhuate. He also reports twenty-three new cases treated by either or both drugs.

He concludes that:

1. Sodium gynocardate is slightly more rapid in its action on anesthetic areas, but that the nodular patches made equally rapid progress. Sodium gynocardate "A" has led to the destruction of the veins in several cases and it was found necessary to give sodium morrhuate. He therefore recommends the following system of dosage in order to obtain the maximum effect: First Week: (1) sodium gynocardate "A" 0.5 c.c. intravenously on the first day; (2) sodium gynocardate "A" 0.5 c.c. to 0.25 c.c. intravenously on the third day; (3) sodium morrhuate 0.5 c.c. intramuscularly on the fifth day.

In this way the dosage should be increased by 0.5 c.c. week by week up to 5 c.c., provided there be no marked febrile reaction or other danger signal. When there is a marked febrile reaction the dose should be halved and again gradually raised, but kept at least 1 c.c. below the dose that produced the marked reaction.

2. In some cases over-dosage led to a marked febrile reaction accompanied by the formation of pustules, and later of sores on the limbs followed by a recrudescence of the anesthesia.

3. In one case there was almost complete recovery but the treatment was stopped too soon and this was followed by a recrudescence of the anesthetic areas.

4. Rapid progress was made at first in several cases followed by slower but steady progress toward recovery. The anesthesia of the face and of the trunk recovered first.

5. Early cases, especially in children, healed up rapidly with intravenous injections of sodium gynocardate "A."

6. As to the length of treatment, the author cannot advise definitely. He thinks, however, that the injections should be continued for some months after the symptoms have entirely disappeared.

GUTIERREZ, Manila.

ARSPHENAMIN AND NEO-ARSPHENAMIN. WILLIAM A. SMITH, J. Lab. & Clin Med. **5**:518 (May) 1920.

In this general article Smith discusses the origin, present supply, rules for manufacture, chemistry, physical properties, technic of administration, reactions and their causes, use in therapeutics and relative value of arsphenamin and neo-arsphenamin. As the supply and rules for manufacture in America are not generally known, the following information should be of interest:

During the war, shipments were stopped, and the supply in the United States was exhausted in 1915. Patent protection was withdrawn in the allied countries, and firms in England, France, Japan and Canada began to manufacture these compounds. After the United States entered the war, the Adamson Bill was passed, granting citizens the right to operate patents owned by enemy aliens. The result was that several products were placed on the market, varying both in their chemical and their physiologic properties. It became necessary to exercise precaution in granting licenses to manufacture these products; for this reason the U. S. Public Health Service defined the properties of good preparations, and the Federal Trade Commission formulated rules and toxicity tests which must be complied with, or the license of the manufacturer may be revoked. The firms licensed at present are:

The Dermatological Research Laboratories, Philadelphia Polyclinic, whose products are called arsphenamin and neo-arsphenamin.

The Takamine Laboratory Co., Inc., New York City, whose products are called arsaminol and neo-arsaminol.

The Farbwerke-Hoechst Co., New York City (at H. A. Metz Laboratories Inc.), whose products are called salvarsan and neosalvarsan.

The Diarsenol Co., Buffalo (Synthetic Drug Co., Toronto), whose products are known as diarsenol and neodiarsenol.

The product of the Dermatological Research Laboratory was known as arsenobenzol, and was found to be identical with salvarsan in composition and equal to it therapeutically, by the Council on Pharmacy and Chemistry of the American Medical Association. This product was made under the direction of Dr. Schamberg, and was first made in this country.

On March 4, 1918, the Federal Trade Commission adopted certain rules for the manufacture of these products; chief among these are:

1. These products are to be named and labeled arsphenamin and neo-arsphenamin, respectively. (Arsphenamin was also previously called arsphenolamin hydrochlorid.)

2. The products are to be sold only in colorless glass ampules, containing an atmosphere of an inert gas.

3. The arsenic content of arsphenamin must be between 29.5 and 31.57 per cent.

4. The arsenic content of neo-arsphenamin must be between 18 and 20 per cent.

5. Each lot must be tested for its arsenic content and toxicity.

6. For toxicity tests, at least four or five albino rats are to be used, non-pregnant, weighing from 100 to 150 gm. A 2 per cent. solution of neutralized arsphenamin in doses not less than 80 mg. per kg. body weight is injected. It is required that 60 per cent. of the animals injected survive at least forty eight hours. Animals are not to be anesthetized for injection and if more than one rat dies, tests are to be repeated. Special rules are given for feeding and caring for the animals used. Tests are also made, on samples submitted, by the U. S. Public Health Service. The Federal Trade Commission can withdraw from the market any lot designated. Detailed records of the tests for each lot are to be kept and furnished to the Federal Trade Commission.

The maximum tolerated dose of neo-arsphenamin must be not below 90 mg. per kg. body weight, with injections of a 2 per cent. aqueous solution, intravenously, at the rate of 0.5 c.c. per minute.

Such restrictions have done a great deal to make the products on the market safe for use and have undoubtedly reduced the number of unfavorable reactions following injection.

ELBERT CLARK, Chicago.

UEBER DAS SKLEROEDEM UND SEINE BEZIEHUNG ZUR SKLERODERMIE (THE RELATION OF SCLEREDEMA TO SCLERODERMA). A. BUSCHKE, Dermat. Wchnschr. **70**:17 (Jan.) 1920.

Buschke gives further observations of the case which he described in 1902 as scleredema (Sklerödem) and also a summary of reports of cases of the same disease which have since been published. He sums up in part the characteristics of the disease thus: "A hardening (Versteifung) of the deeper layers of the cutis, the subcutaneous tissue, and most likely, to some degree the fascia and musculature. The disease apparently begins acutely, in most cases, on the neck spreading on to the face, the upper arms and the trunk to the abdomen. The lower extremities may be involved but seldom are. At the beginning the patients may be affected with weakness and prostration or may feel perfectly well. It has most frequently followed influenza-like affections, scarlet fever and parotitis but it cannot be denied that the former may have been a part of the disease itself. There is no pain, only a feeling of tenseness and rigidity. The movements of the body and breathing may be more or less interfered with by the latter. The skin usually looks pale or infrequently may be slightly cyanosed ,and the upper layers have a velvet-like feel. The induration lies in the deeper parts, has a cartilaginous feel and does not pit on pressure. . . . No disturbances of cutaneous sensations or sweat secretion worth mentioning are present. The full development of the disease may take place rather acutely in weeks or it may take months. It may last months or years but either regresses slowly to complete recovery or apparently some of the induration may remain indefinitely. . . . Histologically the disease shows no inflammatory reaction but is a deposit of a homogenous exudate which presses apart the connective tissue without involving the elastic tissue, the upper layer of the cutis, or the epidermis. There is no atrophy or disturbance of pigmentation. Nothing is definitely known as to the nature of the exudate but Noble has shown that it is not a simple edematous fluid but a deposit of a solid (festen) substance."

Since the genesis of the disease is not clear, the author goes on further to compare it with other similar affections. It differs from diffuse scleroderma in that it has a better prognosis, does not end in atrophy and pigment loss and does not affect the superficial layers of the cutis and epidermis. The author believes that some of the cases of diffuse scleroderma which have had a benign course, healing without permanent changes, are not examples of this disease at all but are scleredema and he cites certain examples from the literature. "Especially in the French literature is the description of acute scleroderma and its course so strikingly like Sklerödem, which Noble has called attention to, that by closer inspection many cases would undoubtedly be found which belong to our disease and should be separated from scleroderma."

Buschke also differentiates it from Fettsklerem (sclerema neonatorum) and from the scleredema of infants (edema neonatorum). He sees, however, a decided likeness between scleredema of adults and the so-called scleroderma of infants, of which only eleven cases have been described, and believes that a portion of the latter at least are examples of scleredema.

KETRON, Baltimore.

TRAITEMENT DE LA SYPHILIS NERVEUSE PAR LES INJECTIONS NOVARSENICALES A PETITES DOSES REPETEES ET PROLONGEES (THE TREATMENT OF NERVOUS SYPHILIS BY REPEATED AND SMALL DOSES OF NEOARSPHENAMIN). J. A. SICARD, Presse méd. (May 8) 1920.

Sicard claims to have obtained noteworthy results in the treatment of tabes, paresis, syphilitic paraplegia and hemiplegia by the daily administration of neo-arsphenamin subcutaneously or intravenously in doses not exceeding 0.15 gm. over an extended period. He has given as much as 50 gm. within a space of two years. He believes this method of treatment to be less dangerous than weekly injections of larger doses and superior in its results in nervous syphilis and in its effect on the Wassermann test in the blood and spinal fluid. He has not observed any nitritoid reactions. Toxic reactions fall chiefly within three groups:

(1) DERMATITIS: Following the injection of from 0.5 to 3 gm. of neo-arsphenamin an erythema occurs in from 6 to 8 per cent. of the cases. It is not of serious significance, and treatment need be interrupted for a few days only. A dermatitis may occur later in the course of injections (5 to 10 gm.) and is of grave significance. It may result in alopecia, keratosis of the palmar and plantar surfaces, ulceration of the skin and mucous membranes, purpura, hemorrhages from the tongue, tonsils and pharynx. Sicard believes that certain lots of arsphenamin are more apt to produce this serious reaction.

(2) LOSS OF ANKLE JERK: In about 60 per cent. of cases following the administration of from 7 to 10 gm. of neo-arsphenamin there is a progressive diminution of the ankle jerks leading to its complete and permanent abolition. There is no muscular weakness or sensory changes with the exception of formication in the toes and soles in occasional cases. In only one case was the patellar reflex abolished. These changes exert a favorable influence in spastic paraplegia.

(3) ICTERUS: This occurs in about 2 per cent. of cases and is benign, disappearing in from three to four weeks.

ZIMMERMANN, Baltimore.

ECZEMATOID EPIDERMOPHYTON INFECTION IN CHINA. H. DOLD, China M. J. **33**:133 (March) 1919.

Dold found many cases of inflammation of the feet of the type he calls eczematoid inflammation of a vesiculopustular, dysidrotic type. He found this condition common among the Chinese, but seldom found it among white foreigners living in China. His cases are similar to those in European countries and in America, except that in his cases the process spreads to the plantar and dorsal regions and finally covers the whole or almost the whole surface of the foot. He classifies his cases into four main types: (1) the vesicular type, a sudden appearance of a sago grain-like vesicular eczema accompanied by intense itching; (2) chronic intertriginous type, desquamation of the skin in the peripheral zones and formation of whitened sodden masses of epithelium between the toes; (3) chronic hyperkeratotic type, formation of masses of overgrown horny layers, especially on the plantar surface; (4) pyodermic type, due to secondary infections.

The disease is more common in the southern part of China and more frequent during the summer. The condition heals or at least diminishes during the winter months and recurs in the summer. Some cases persist throughout the year.

In ninety-four of ninety-eight cases the disease occurred only on the feet; in two cases only on the hands; in two cases only in the genitocrural region; in one case on the feet and one hand, and in another case both feet and the right axillary region were simultaneously affected.

Microscopic examinations were done in all of the ninety-eight cases and in ninety-five the fungi could be demonstrated. Repeated examinations of the lesions should be made in those proving negative on the first examination.

Culture in Sabouraud's medium was tried in thirty-one cases and in only fourteen cases was the attempt successful. Dold considers the fungus identical with the one of Sabouraud's *Epidermophyton inguinale*.

He thinks that the disease in question is caused by *Epidermophyton inguinale* (Sabouraud) and the condition described by Martin Costa in Brazil, by Castellani in Ceylon (dermatitis rimosa of the toes) and by Cantlie in Hongkong ("Foot-tetter," "Dermatitis bullosa plantaris") are manifestations of infections with the same or closely related fungi.

Experimental transmission has been produced by him on two occasions from a pure culture of the organism.

GUTIERREZ, Manila.

LE CANCER DE LA DERMATOSE PRECANCEREUSE DE BOWEN (THE CANCER OF THE PRECANCEROUS DERMATOSES OF BOWEN). J. DARIER, Ann. de dermat. et syph. **1**:49, 1920.

Darier is impressed with the fact that aside from the primary cancers of the skin, such as the spinocellular epithelioma, basal cell epithelioma and novocarcinoma, we meet types of cutaneous epithelioma which differ from the above in clinical evolution and histologic structure. In this group should be included the cancer developing in the precancerous dermatosis of Bowen, and Darier feels that the latter condition will be found frequently as it becomes better recognized. Darier describes a case in which almost the entire face was involved by a vegetating dermatosis with carcinomatous change. Diagnosis was difficult, and vegetating tertiary syphilis,

tuberculosis, pemphigus vegetans, some mycotic disease and an unusual type of epithelioma had to be considered. The latter diagnosis was finally established. The features which differ from spinocelled epithelioma were the absence of pearly margins, the relative softness and particularly the great superficial extension without deep adherence, while the rapid progress and early glandular involvement did not conform to the picture of basal cell epithelioma. As the patient died the author gives detailed necropsy and histologic findings. Darier concludes that the cancer of the precancerous dermatosis of Bowen has clinical and histologic characteristics so well defined that a diagnosis can be made even in the absence of history of the beginning and evolution of the condition.

Clinically, the distinguishing features are its superficial rather than deep extension, its vegetating rather than ulcerative tendency; the formation of circumscribed plaques of conglomerated excrescences, separated by deep furrows, covered with scaly crusts and stippled with white points resembling milium. Its extension is rapid; it can produce profuse hemorrhages; it is accompanied by adenopathy, the glands being small, multiple and discrete; the metastases are lymphatic and can give rise to visceral involvement. The histologic structure is still more characteristic, and is given in detail.

Radical and early treatment is advised, surgical measures being preferable.

SENEAR, Chicago.

## FURTHER INVESTIGATIONS ON THE CHEMICAL NATURE OF MARGOSIC ACIDS (FATTY ACIDS OF THE NIM OR MARGOSA OIL). RECENT CONCLUSIONS DRAWN FROM EXPERIMENTAL AND CLINICAL USE OF MARGOSATES AND ETHYL ESTER MARGOSIC. K. K. CHATTERJEE, Indian M. Gaz. **54**:171 (May) 1919.

After discussing the chemical properties of this drug, Chatterjee takes up the action of the ethyl esters margosic and margosates. Chatterjee thinks the antisyphilitic properties of margosates are due to their being soaps of a special kind as they contain a fatty acid of a peculiar chemical formula. Soap acts chiefly by a process of hydrolysis induced either by its coming in contact with water or by the enzymic activity of the fluid tissues of the body. Ethyl ester margosic has these two characteristics: 1. It is in loose chemical combination and therefore is more readily hydrolyzed than potassium margosate. 2. Its margosic content is higher than that of potassium margosate.

Chatterjee thinks it not unlikely that concurrently with the process of hydrolysis the lipoid-globulin or the protective substance of the serum is broken up and the organism of syphilis is set free. It is possible for the organism to be hydrolyzed but in clinical conditions this renders the organisms inert and only in some instances is the destruction complete. Hydrargyri margositas was therefore introduced, combined with the ester. The metallic mercury is liberated and becomes fixed to the hydroxyl groups and so alters the arrangement of its ions that the protoplasm is disintegrated and the parasite killed.

Chatterjee then discusses the action of the drug on syphilis, leprosy, skin disease, filariasis, septic infections and ulcers.

Of twenty-seven cases of syphilis treated with potassium margosate, ethyl ester margosic and ethyl ester margosichydrargyri margositas, the lesions disappeared most quickly by the treatment of ethyl ester margosichydrargyri margositas.

Cases of Leprosy: Tuberculous, maculo-anesthetic and mixed types have been treated. In three patients the treatment has been suspended; eight are still under treatment. In the first three cases treatment was commenced with potassium margosate. One of these gave up treatment after making satisfactory progress. The other two patients made steady progress with potassium margosate, but progress was more marked and rapid after ester treatment was commenced.

Patients with skin disease have been treated with satisfactory results. The following conditions have been treated: eczema, erythema iris, scleroderma (localized), tinea affections, pedicular conditions of the scalp and trunk, scabies, erythrasma, dermatitis (exfoliative and ulcerative) and diffuse psoriasis.

GUTIERREZ, Manila.

A CASE RESEMBLING YAWS. A. J. NORONHA, Indian M. Gaz. **54**: 178 (May) 1919.

Following an injury from a broken bottle, a Hindu lad, aged 15 years, had an ulcer and granulations. One month or so after this accident he noticed a scattered eruption all over his body. On examination he was found to have round his anus and over the scrotum extensive condylomas and also scabies on the trunk, genitals and extremities. Raised condylomatous yellowish patches, the size of a split pea, were present on the forehead, lips, trunk and extremities. These were all uniform, differing only in size. The Wassermann reaction was ++++.

GUTIERREZ, Manila.

LA SYPHILIS NEUROTROPE, EXISTE-T-ELLE (IS THERE NEUROTROPHIC SYPHILIS)? MAURICE PAGE, Presse méd. **28**:447 (April) 1920.

According to Page, two distinct types of syphilis exist, the ordinary syphilis "dermatrope" which may give rise to tabes and general paralysis, but rarely and with special characteristics, and a special type of syphilis "neurotrope" having an affinity for the nervous system. The difference is due to a variation in the spirochete itself and not to a predisposition on the part of the affected tissues. He calls attention to the scarcity of skin, mucus and bone tissue involvement in the neurotropic type. The husband or wife of the diseased one often is not infected. The children of tabetic and paretic persons, although showing a certain psychic disharmony, are usually exempt from hereditary syphilis.

Because of the difficulty of impregnating the nerve cells with antisyphilitic treatment, the author has conceived the idea of adding to the treatment the action of a serum or a toxin. He gives three injections of animal tuberculin and follows this with six doses of novarsenobenzol or arqueritol (interval not given). Collin prefers the serum of Marmoreck or the serum of Roux can be given. The object of the preliminary injections of a serum or toxin is to produce a "cataclysme de l'organisme" destined to cause a discharge of opsonins and a leukocytosis as great as possible, so that the arsenic or mercury will have a better chance of reaching the nervous substance. The author admits that further time is necessary to prove the value of this method of procedure.

KETRON, Baltimore.

ANTE-NATAL AND POST-NATAL SYPHILIS. JOHN ADAMS, Brit. M. J. **1**:603 (May 1) 1920.

At a meeting of the Hunterian Society, Adams demonstrated a number of cases that had been treated at the Venereal Disease Center for Pregnant Women.

In the two years 1917 and 1918, fifty-eight mothers were treated. Twenty-five of the babies gave a positive Wassermann reaction at birth, and twenty-seven gave a negative reaction. There were six still-born babies. Adams concludes that treatment of pregnant women could be carried up to the day of confinement with safety and success, and a mother so treated might give birth to a baby with a negative Wassermann.

The treatment of syphilitic infants began immediately after birth, and consisted of the combined injection of galyl in glucose, and gray oil. Children so treated became healthier, put on weight, and their blood became negative and remained so.

This method was used: A dose of 1.5 cg. is injected into one buttock on the day after birth, and repeated after one week. The dose is gradually increased up to 5 cg. Hydrargyrol with chalk is given by mouth and intramuscular injections of gray oil, beginning with ¼ grain and increasing up to ½ grain, are given every two weeks to the babies and to the mothers once a week.

Adams says that as a general rule, with this combined treatment the Wassermann test is negative about the seventy-eighth day.

OLIVER, Chicago.

MEDICAL NEWS FROM KANSU. G. E. KING, China M. J. **33**:38 (Jan.) 1919.

Kansu is immediately south of the Mongolian plateau, with a population of from 5,000,000 to 10,000,000. Incidence of disease is influenced in the central part by the presence of Tibetians, and in the northern by Mongolians.

Smallpox, occasional epidemics of diphtheria, measles, mumps and scarlet fever occur. Scarlet fever is regarded as a disease newly imported to China. Malaria is not present in the northern zone. Some parts of the province show much goiter, which the native regards as due to the drinking of spring water or the water of mountain streams.

Leprosy is rare in a greater part of the province, but on the Tibetian border, in the center of Toochon, Howchow and Sinay it is known and feared.

The most common form of carcinoma is epithelioma over the trochantor induced by irritation from sleeping on the hot K'ang. Of tropical diseases, there are cases which resemble kala-azar; elephantiasis of the lower limbs has been observed.

One disease that the author wished diagnosed is what he calls progressive congenital angioma. The patient was 25 years old. A nodule the size of a bean, hard and of dark blue color was first noticed on the scapula. It grew slowly and painlessly till it attained the size of a pear. Other lesions appeared and the disease progressed in exacerbations annually in the spring and autumn. Intense varicosity of the vessels of the left arm and scapular region are now present. The bones and muscles are atrophied.

GUTIERREZ, Manila.

INFECTIONS AND VACCINES. PAUL G. WOOLEY, J. Lab. & Clin. Med. **5**:543 (May) 1920.

"Vaccination has for its aims: (1) The initial increase of resistance of the host so that invasion by bacteria is made more dfficult or, in the extreme case (smallpox), impossible. (2) To so modify the fluids of the body that once an organism has invaded the body it is not able to survive the condition which discourages parasitism (typhoid). (3) To so modify the fluids that in the case of developed parasitism, the bacteria are eventually killed (furunculosis). It is this latter instance in which we are especially interested at this time."

Autogenous vaccines are to be preferred to stock vaccines. The value of mixed vaccines, even though autogenous, is questionable and their use unscientific. It were more advisable to use a known unmixed stock vaccine, a carefully studied polyvalent vaccine, or a single purified protein.

"Finally, and as practically as possible, vaccines (autogenous) seem to be useful in the following infectious disorders:

"(1) Furunculosis and localized abscesses in soft tissues; (2) acne vulgaris; (3) colon bacillus, pyelitis and cystitis; (4) chronic gonorrhea and gonorrheal rheumatism; (5) chronic bronchitis; (6) bronchial asthma of bacterial origin.

"Vaccines seem to be of little or no value in (1) infection of bone or infections in cavities with rigid walls; (2) infection of the intestinal tract; (3) infection of the uterus and adnexa.

"Vaccines are contraindicated in (1) acute infections and infectious diseases; (2) septicemia and pyemia in the acute stages; (3) malignant endocarditis."

ELBERT CLARK, Chicago.

THE VALUE OF LUETIN IN AN OUTPATIENT DEPARTMENT. ALFRED E. MEYERS, Arch. Pediat. **37**:223, 1920.

The writer in an interesting article, records his experience with injections of luetin in the Outpatient Pediatric Department of the University of California Medical School. Feeling that every case of hereditary syphilis, whether active or latent, would show some stigmas of abnormal development, Wassermann and luetin tests were made on every child who did not score 100 from a developmental standpoint. The reason for their coming to the clinic, as well as the suspicious points in their history or physical examination, were noted. One hundred and sixty-eight cases were tested; 61 per cent. were males, 39 per cent. females. The oldest child was 18 years, the youngest 7 weeks. The Wassermann and luetin tests were both positive in 17.8 per cent.; the Wassermann negative and the luetin positive in 47.6 per cent.; both were negative in 28.5 per cent. The total number of positive reactions was 65.4 per cent., and in practically every case that gave a positive luetin reaction, there was something in the physical findings or the history indicative of syphilis. The majority of reactions were of the papular type; after forty-eight hours there appeared at the site of injection a definitely indurated papule, from 5 to 12 mm. in diameter, surrounded by a zone of redness.

The author's conclusions are:

1. The luetin test is more reliable in congenital syphilis than the Wassermann test.

2. At least 65 per cent. of congenital syphilitic patients will react positively to the test.

3. It causes no constitutional reaction.

4. It is more important to do a routine luetin test in the clinic than the von Pirquet test, providing the material can be obtained.

OLIVER, Chicago.

CONTRIBUTION A L'ETUDE DE LA PATHOGENIE DU SOL-DISANT SYPHILOME ANO-RECTAL, FOURNIER (CONTRIBUTION TO THE STUDY OF THE PATHOGENICITY OF THE SO-CALLED ANORECTAL SYPHILOMA OF FOURNIER). O. JERSILD, Ann. de dermat. et de syph. **1**:62, 1920.

Jersild carefully reviews the question of the anorectal syphiloma of Fournier, gives the detailed findings in six cases observed by himself, and concludes:

1. All findings show that patients with characteristic lesions of this type are syphilitic.

2. The fixed localization of the rectal infiltration indicates an affection anatomically determined.

3. The pathogenic mechanism is as follows: (*a*) Some lesions (chancre, chancroid, etc.) of the anoperineal region, with inguinal lymphadenitis, arrest of the lymphatic circulation in the inguinal glands or in the afferent lymph vessels of the glands. (*b*) Turning of the lymph of the anogenital region by the rectal lymphatics toward the glands of the mesorectum. (*c*) Anorectal adenitis (obliteration posteriorly). (*d*) Lymphatic stasis between the two obliterations mentioned in (*a*) and (*c*).

SENEAR, Chicago.

ZUR DIAGNOSE UND THERAPIE DES BENIGNEN MILIARLUPOIDS (BOECK) (THE DIAGNOSIS AND TREATMENT OF THE BENIGN MILIARLUPOIDS [BOECK]). GERTRUDE V. BOMBARD, Dermat. Wchnschr. **70**:161 (March) 1920.

The author describes a case showing the three forms—small nodular, large nodular and diffuse infiltrating—of miliarlupoid. The patient was a woman, aged 33, and the eruption was limited to the face and upper extremities. There was glandular enlargement and chronic nephritis and roentgen-ray examination revealed a small infiltration in the lungs and changes in the bone and periosteum of the left upper arm. The Sachs-Georgi reaction was positive. Wassermann and Pirquet reactions were negative. Animal inoculation with material obtained at biopsy gave negative results. The author believes from her observations of this case that benign miliarlupoid is clinically and histologically a well defined, bacillary, general disease which is most likely a special, mild form of tuberculosis.

The case was treated with intravenous injections of "Silbersalvarsan" but without improvement. Krysolgan ( a gold preparation prepared by A. Feldt) was then tried and after several injections the skin lesions as well as the periosteal thickening disappeared, leaving only the telangiectasia. The lung condition, however, showed no improvement and was perhaps worse.

KETRON, Baltimore.

EINE TUBERCULINREACTION DER LYMPHGEFAESSE (A TUBERCULIN REACTION OF THE LYMPH VESSELS). ENGWER, Dermat. Wchnschr. **70**:188 (March) 1920.

The author describes a case of tuberculosis verrucosa cutis on the hand in which there had been transplantations by way of the lymphatics up the arm. A tuberculin test on the affected arm had caused an acute inflammatory reaction in the affected lymph vessels.

KETRON, Baltimore.

SOME SURGICAL ASPECTS OF SYPHILIS. W. P. COUES, Boston M. & S. J. **182**:582 (June 3) 1920.

The author emphasizes the worthlessness of a negative report on a routine Wassermann test and the value of skeletal radiography as a help in latent syphilis. He calls attention to certain conditions in which syphilis is masquerading as a surgical condition complicating a surgical case:

1. Cervical adenitis due to tertiary syphilis is mistaken for tuberculous adenitis and Hodgkin's disease.

2. Deep seated syphilitic mediastinitis is sometimes mistaken for hopeless malignant disease.

3. Obscure conditions simulating ordinary bursitis or synovitis are quickly cured symptomatically when a proper diagnosis is made.

4. Syphilitic bone disease at times underlies varicose veins of the legs and varicose ulcers. Not infrequently specific ulcers of the leg are diagnosed as varicose because the patient has varicose veins.

5. In nonunion and delayed union of fractures, and repeated fractures from slight trauma, the possibility of syphilis must always be borne in mind. The author mentions one clinic in which every case of ununited fracture for a year gave a positive Wassermann reaction.

6. Gummatous infiltration of the testicle is not infrequently operated on for sarcoma, teratoma or tuberculosis, and is often confused with an enlargement due to the gonococcus.

7. Tabetic arthropathies, with or without ulceration, are not infrequently incorrectly diagnosed, especially ulcer on the sole of the foot.

8. Five or six per cent., or possibly more, of ulcers of the stomach are now said to be syphilitic.

LANE, Boston.

ZUR FRAGE DER GIFTFESTIGKEIT DER SPIROCHAETEN (RESISTANCE OF SPIROCHETES TO DRUGS). GUSTAV FANTL, Dermat. Wchnschr. **70**: (Feb.) 1920.

Stejskal (*Dermat. Wchnschr.*, 1919, No. 41) had shown that arsphenamin caused spirochetes to disappear less rapidly from lesions of patients who had previously received mercury than from those of untreated cases and concluded that the organisms developed a resistance to arsphenamin as a result of the mercurial treatment. Fantl's experiments supported this conclusion. Spirochetes derived from mercury-treated patients (mercuric chlorid and salicylate intramuscularly) remained motile in dark field preparations for a longer period than from untreated cases. In the untreated cases the average duration of motility was fourteen hours in contrast to twenty hours in the treated. Resistance was also tested by the effect of adding arsphenamin (0.01 per cent.)

and mercuric chlorid (0.2 per cent.) to serum in dark field preparations. The spirochetes from untreated cases lost their motility within a short time, while those from treated cases remained motile for hours. The data from only a few cases are given in detail.

ZIMMERMANN, Baltimore.

ORIENTAL SORE OR BAGDAD BOIL. D. J. HARRIES, Indian M. Gaz. **54**:325 (Sept.) 1919.

Harries discusses the modes of transmission and relationship between kala-azar and oriental sore, saying that the organisms found in the sore are indistinguishable from those found in kala-azar. He further points out that patients suffering from kala-azar do not suffer from oriental sore, and thinks that the patient is rendered immune from the presence of one or the other.

After discussing the various symptoms and phases of the disease, he outlines a course of treatment as follows:

Internal: The best results have been obtained by intravenous administration of a 1 per cent. solution of antimony tartrate, starting with 5 c.c. and gradually increasing the amount to 10 or 15 c.c. It may be given daily or every other day.

Local Measures: (1) Local application of antiseptic solutions, (2) ionization, and (3) complete excision. Complete excision has given the best results. When the sores are localized it is the method of election, but when they are multiple other methods should be resorted to.

GUTIERREZ, Manila.

UEBER DER HISTOPATHOLOGIE DER DRUSENERVEICHUNG IN FRUHSTADIUM DER LUES (THE HISTOPATHOLOGY OF GLAND SOFTENING IN EARLY SYPHILIS). A. FINSTERLIN, Dermat. Wchnschr. **70**:97 (Feb.) 1920.

Finsterlin examined the inguinal glands of a patient with multiple chancres in which softening of the glands could be explained only on the basis of syphilis. The fluid from the fluctuating glands was negative on bacteriologic examination. He emphasizes the following changes: mesarteritis, new capillary formation, plasma cell infiltration and areas of necrosis in the central portion of the glands. He attributes the necrosis to pressure on the vessels by the dense infiltration, a process analogous to that in chancres and in the bubonuli occurring along the dorsal lymph vessels of the penis. Individual resistance must also be taken into consideration.

ZIMMERMANN, Baltimore.

TREATMENT OF PRURITUS ANI BY X-RAY RADIATION. WILLIAM J. YOUNG, Am. J. Roentgenol. **7**:116, 1920.

Young relates briefly his experience in treating pruritus ani with roentgen ray. The results for the most part have been commendable. Unfiltered doses of roentgen ray were used.

In the treatment of pruritus ani during the last four years he has depended entirely on fractional doses of roentgen ray given at weekly intervals, the dosage being governed by the infiltration of the anal tissues, from four to ten radiations constituting the treatment. In the cases treated, the results have varied from temporary improvement to seeming cure. His best results have been secured when working in conjunction with the proctologist, his

part consisting of relieving the pruritus while the proctologist tried to correct the particular condition that operated as a causative factor.

His experience has been that recurrence of the pruritus depends on the amount of rectal pathology present.

ELBERT CLARK, Chicago.

THE DEEPER STRUCTURAL CHANGES ARISING FROM VARICOSE ULCERATION. DUDLEY H. MORRIS, Surg., Gynec. & Obstet. **30**:72 (Jan.) 1920.

It is unusual for a periostitis or osteomyelitis to localize beneath an ulcer. Instead, far reaching changes such as a diffuse periostitis or osteomyelitis of the tibia, fibula or both these bones develops, which is so diffuse as to extend throughout the entire shafts and involve even the epiphysis, and so chronic as to pass unnoticed by the patient. The inflammatory process apparently never reaches the stage of abscess formation, and if suppuration exists its products are absorbed into the system. Widespread vascular changes accompany this. The deep vessels, posterior tibial and peroneal show marked calcification which extends to the popliteal or above, and which occurs independently of the ulcer, but is most marked in those cases in which ulceration has been present for a long time.

The mechanism of the bacterial distribution to the parts of the bone remote to the ulcer is by way of the arterial wall and adjacent lymphatics.

Photographs of cases and of roentgenograms of the leg bones accompany this excellent and significant article.

GOODMAN, New York.

ON THE HISTOLOGICAL RESEMBLANCES OF ORIENTAL SORE TO EPITHELIOMA. WILLIAM MACADAM, Brit. J. Surg. **7**:28, 1919.

Macadam states that in examining a number of excised skin lesions of the type of Oriental sore he found that most of them showed the character of a chronic ulcer, but in two of them the histologic picture was practically indistinguishable from a squamous-celled carcinoma.

The first specimen of the latter two was taken from an ulcer of three months' duration in which typical *Leishmania tropicum* bodies were found. The accompanying drawing shows a picture closely resembling epithelioma, but with considerable round cell infiltration. The other specimen presenting a similar histologic picture, was taken from an ulcer on the lip.

Macadam notes that there is a possibility that some of these ulcers in their chronicity may take on the characters of true carcinoma, but he found no clinical evidence of such a change in the two cases cited. He also calls attention to the fact that in sores of some duration, in which early malignancy may be a probability, it may be impossible to detect the *Leishmania tropicum*, since the parasites tend to disappear in lesions of some months' standing.

SENEAR, Chicago.

AUTOPLASTIC SURGICAL TREATMENT OF BALDNESS. R. PASSOT, Presse méd. **28**:222 (April 17) 1920.

Passot reports a method of treating baldness by plastic operation. He takes pedunculated flaps from the hairy part of the scalp and moves them over to the bald areas. He reports successful results in six cases so treated.

TREATMENT OF SYPHILIS BY ANTISYPHILITIC SERUM OF QUERY. J. Dobriansky and T. Thompson, Lancet, **1**: 903 (April 24) 1920.

Dobriansky and Thompson give a brief report on this interesting subject. Query serum is prepared by inoculating monkeys with filtered cultures of *Spirochaeta pallida* on bouillon. When the monkeys so infected give a strong positive Wassermann reaction, they are bled and the serum is preserved in ampules. Dobriansky and Thompson report three cases of syphilis treated with this serum with great improvement. They are said to have been cases in which established methods of treatment had failed to relieve symptoms. One was a case of gummatous ulcers of the leg; the second a case of tabes with ataxic symptoms, and the third a tabes with lightning pains.

AN UNUSUAL CASE OF KELOID. Rutherford Morison, Brit. J. Surg. **7**:28, 1919.

Morison reports a case of keloid occurring in a negro, the lesion developing on the ears at the site of openings made for ear rings. In the photographs each of the tumors appears as large as the patient's head. Morison recalls that keloids are associated in some way with sepsis and chronic tuberculosis, and that on the skin burn scars and scars resulting from tuberculosis are their favorite sites. He believes that it is not generally recognized that similar growths are to be found elsewhere in the body, and he cites a number of such instances in lesions of the mouth and the gastrointestinal tract.

Senear, Chicago.

A CASE OF GENERALIZED ALOPECIA OF NERVOUS ORIGIN. Carlo Todde, Riforma med. **36**:382, 1920.

The author presents the case of a lieutenant in the Italian army, a man of 34, who after severe nervous shock caused by continuous bombardment during seven days, noticed the rapid falling out of his hair, accompanied by slight pruritus. The alopecia began on the head and soon spread to the eyebrows, beard and the rest of the body. In a few days the baldness was complete and generalized. The patient denied syphilis. The Wassermann test was negative. The observer could rule out ringworm, infectious diseases and other diseases that may produce alopecia. He thinks this case the result of intense nervous strain and violent emotions, which, perhaps, led to disturbances of the internal secretions, affecting the nutrition of the hair. Accordingly the author treated the patient with extracts of endocrinous glands. The final therapeutic results are not reported.

V. Pardo-Castello, Havana.

DIE SYSTEMATISCHE KOMBINIERTE STRAHLENBEHANDLUNG DER HAUTTUBERKULOSE, INBESONDERE DES LUPUS (THE SYSTEMATIC COMBINED RADIATION OF SKIN TUBERCULOSIS, ESPECIALLY LUPUS). G. A. Rost, Dermat. Wchnschr. **70**: 129 (Feb.) 1920.

The method described by the author consists of the combined use of the roentgen ray, ultraviolet light (Kromayer lamp) and artificial sunlight. The affected area was given a full roentgen-ray dose about every six weeks with a 1 to 4 mm. aluminum filter. The ultraviolet light treatments, with blue glass

filter, were given between the roentgen-ray treatments at somewhat more frequent intervals. The reaction was allowed to disappear entirely before a roentgen-ray treatment was given. Besides this local treatment, the patients had general applications of artificial light (Künstlicher Höhensonne). These light baths exerted a good effect on the local disease, but the method by which this was accomplished is not known; an increase of the protective substances in the skin is a possibility. The author believes that pigmentation is not to be desired since it decreases the absorption of the light rays. The treatments were given about twice weekly, producing an erythema but no vesiculation. The time of treatment was prolonged as pigmentation increased but no treatments over thirty minutes long were given. When the pigmentation became great a depigmentation pause of several weeks was allowed.

KETRON, Baltimore.

SEPTIC FEVER OR SYPHILITIC SEPTICEMIA. D. McCOY, Indian M. Gaz. **54**:260 (July) 1919.

McCoy reports three cases in which the cause of the fever could not be determined. It was septic in character, not influenced by quinin. There was history of syphilis in all three cases, though gonorrhea was admitted by the patient in Case 1. The same patient had had several attacks of fever of the same character as the present while in German East Africa. There were no signs of syphilis in the three patients.

In these patients the fever subsided immediately after the administration of antisyphilitic remedies. The Wassermann reaction was positive in all three.

GUTIERREZ, Manila.

ENQUETE SUR LA FREQUENCE DES TUMEURS MALIGNES DE LA PEAU CHEZ LES INDIGENES NORD-AFRICAINS (FREQUENCY OF MALIGNANT NEOPLASMS OF THE SKIN AMONG THE NATIONS OF NORTHERN AFRICA). J. MONTPELLIER and H. MARCHAND, Bull. Soc. franç. dermat. et syph. No. 8, 317, 1919.

Montpellier and Marchand offer the observations of J. Brault in contradiction to the established idea that malignant neoplasms of the skin are rare or almost nonexistant among the natives of North Africa, and state that efforts are being made to collect statistics of the frequency of various types of malignant neoplasms of the skin as they occur in this region.

SENEAR, Chicago.

ARSPHENAMIN REACTIONS. JOHN F. MARTIN, J. A. M. A. **74**:18 (May 1) 1920.

The sequelae arising from arsphenamin medication may be thus classified: the incidents, slight untoward symptoms occurring in patients with normal tolerance to arsphenamin, such as vertigo, palpitation, disturbance of taste and smell, or slight nausea; the reactions, usually occurring in syndromes, and causing discomfort and sometimes incapacity, which may be ascribed to allergic or acquired susceptibility to arsphenamin, functional or organic complications, or toxic arsphenamin solutions; the grave reactions (sometimes fatalities), such as dermatitis exfoliativa, toxic jaundice, hemorrhagic encephalitis and gangrene; the accidents, such as thrombosis, phlebitis, and infiltrations about a vein.

LEVIN, New York.

TOKELAU (T. IMBRICATA). H. Jouveau-Dubreuil, China M. J. **33**: 223 (May) 1919.

Joveau, contrary to general conceptions that this disease is confined to warm countries and near the sea, found several cases of it in Szechwan which is far inland and where the climate is continental and temperate. He gives a good description of the disease and his method of treatment. This in brief consists in the application of a 10 per cent. ointment of chrisophanic acid to the legs and if the patient does not show any signs of poisoning the medicine is applied to the trunk and to the neck. He even treats the face with the drug, taking care not to get the ointment into the eyes.

Gutierrez, Manila.

CAUSES DU SYNDROME MALIN DANS LA SYPHILIS (CAUSES OF MALIGNANT SYPHILIS). G. Lacapere, Bull. Soc. franç. dermat. et syph. No. 8, 320, 1919.

As a result of observations made among the Arabs, Lacapere feels that malignant syphilids are the result of vascular hypotension, the latter usually being due to malaria in the cases studied. Among the better classes tuberculosis, anemia, etc., may produce this hypotension. He does not believe in the invocation of a malignant strain of spirochetes to explain these cases.

Senear, Chicago.

UEBER AORTENVERAENDERUNGEN BEI LATENTER LUES (CHANGES IN THE AORTA IN LATENT SYPHILIS). Erwin Pulay, Dermat. Wchnschr. **70**:177 (March) 1920.

Examination of latent syphilitics in a dermatologic clinic revealed eighty-five patients with aortic changes, forty-six men and thirty-nine women. The interval between infection and discovery of signs of aortitis varied from one to fifty years. Pulay advocates repeated examination of every syphilitic for signs of aortitis so that early and thorough treatment may be instituted. Roentgenology is most important and in many cases will be the only means of detecting the aortitis.

Zimmermann, Baltimore.

OBSERVATIONS ON THE COLLOIDAL GOLD REACTION WITH CEREBROSPINAL FLUID. Ellis Kellert, Am. J. Med. Sc. **159**:257 (Feb.) 1920.

Attention is called to the fact that this reaction may at times be false and misleading and a number of cases are cited to illustrate the point. In seventy-five cases with negative reactions, 7 per cent. were false; 70 per cent. of positive syphilitic reactions had positive Wassermann reactions, while 6 per cent. had a positive gold curve and a negative Wassermann reaction. In tuberculosis 88 per cent. of reactions were correct, in acute meningitis 80 per cent. being most valuable in determining a cerebrospinal syphilis. Other diagnostic means should also be used to confirm these findings before treatment is begun.

It was found that spinal fluid contaminated with blood even in very small quantities could give a syphilitic curve and that positive results should be supported by other positive findings to be of value. The writer concludes by stating that he considers the Wassermann reaction and cell count in the spinal fluid to be of greater value than the colloidal gold curve.

Jamieson, Detroit.

RADIUM IN KELOID AND CAULIFLOWER GROWTHS ON SAME FOLLOWING EXTENSIVE BURNS. HARRY B. KURTZ, Urol & Cutan. Rev. **24**:4 (April) 1920.

The writer reports the occurrence of deforming keloids in a man who had been burnt by hot lead. During the course of four months 5,000 mg. hours of radium was applied with ultimate cosmetic improvement.

LEVIN, New York.

BEITRAGE ZUR DIFFERENTIALDIAGNOSE ZWISCHEN PSORIASIS UNIVERSALIS UND DEN EXFOLIATIVEN ERYTHRODERMIEN (THE DIFFERENTIAL DIAGNOSIS BETWEEN GENERALIZED PSORIASIS AND EXFOLIATIVE ERYTHRODERMIAS). H. W. SIEMENS and JULIUS THIEME, Dermat. Wchnschr. **70**:9 (Jan.) 1920.

The author describes at length a case of universal psoriasis and takes up briefly the differential diagnostic points.

KETRON, Baltimore.

THE ETIOLOGY OF THRUSH. A. CASTELLANI, J. Trop. M. **23**:17 (Jan. 15) 1920.

The author believes thrush is not such a simple condition as has been thought, but is due to a variety of fungi and not to the one variety of *Monilia albicans* (Robin) He recognizes two types of lesions—the white or gray-white and the yellow or yellow-brown, the latter being of rare occurrence.

JAMIESON, Detroit.

GROUPED COMEDONES IN AN ADULT. E. G. GRAHAM LITTLE, Proc. Roy. Soc. Med. **13**:39 (March) 1920.

An eruption closely simulating acne vulgaris developed on the chest following the local application of camphorated oil.

GUY, Pittsburgh.

CASE OF CORNUA CUTANEA OF THE FEET. A. M. H. GRAY, Proc. Roy. Soc. Med. **13**:57 (March) 1920.

A case of cutaneous horns developing on the side of "corns" is discussed.

GUY, Pittsburgh.

NERVE DEAFNESS DUE TO CONGENITAL SYPHILIS. M. B. KAY, J. A. M. A. **74**:1162 (April 24) 1920.

Kay reports three cases in which syphilis produced deafness in all three children of one family in the same manner, every other part of the body escaping but the eighth nerve. Owing to the fact that at least a year had elapsed before signs of deafness developed, Kay believes that these were undoubtedly cases of "late hereditary syphilis." Each of the children was put on increasing doses of potassium iodid, reaching 35 grains, three times a day. The general result has been good.

WAUGH, Chicago.

CASE OF LICHEN PLANUS AND PSEUDOPELADE. S. E. Dore, Proc. Roy. Soc. Med. **13**:13 (Dec.) 1919.

A woman, aged 28, presented lesions of lichen planus and pseudopelade. In discussing the case Dr. Whitefield expressed the opinion that more than one disease is included under pseudopelade or cicatricial alopecia. One condition, in which there is scarring with alopecia, he considers a scleroderma. The other condition, in which there is no scarring or obvious atrophy, he considers a probable infective process and suggests strong antiseptics and a guarded prognosis.

Guy, Pittsburgh.

CONTRIBUTION A LA TECHNIQUE DE LA REACTION DE WASSERMANN (CONTRIBUTION TO THE TECHNIC OF THE WASSERMANN TEST). M. Goubeau, Bull. Soc. franç. de dermat. et syph. **7**:265, 1919.

Goubeau presented before the Society Lagage's opinion of the Wassermann reaction and stated that the latter believes the principal cause of contradictory results in the test is faulty titration of complementary power of serum. Lagage also proposes: (1) a common antigen which has been carefully titrated; (2) abandoning the "drop" method of measuring, and (3) the use of colorless human serum from patients who have not eaten recently.

Senear, Chicago.

A SIMPLE METHOD OF CULTIVATING THE MICRO-ORGANISMS OF ACTINOMYCOSIS. M. H. Gordon, Brit. M. J. **1**:435 (March 27) 1920.

The actinomycosis fungus can be readily cultivated in ordinary nutrient broth to which a few drops of fresh human blood have been added. It is advisable to sow the material in two blood mixtures, one of which is covered by a layer of oil, 1 cm. deep. After incubation for a few days at 37 C. the actinomyces fungus can be seen growing at the foot of the tube in small white masses. As a rule, growth occurs first in the broth covered with oil, but when other bacteria are present the actinomyces may come up first in the aerobic tube.

Vaccines may be prepared and used successfully.

Goodman, New York.

SILVER SALVARSAN. H. Boas and A. Kissmeyer, Ugesk. f. Læger **82**: 196 (Feb. 5) 1920; Idem., A. Korsbjerg, p. 196.

Boas and Kissmeyer report good results in sixty-two cases of syphilis treated with silver arsphenamin. They think it is as effective as the old arsphenamin and more soluble. Korsbjerg writes on the same subject, reviewing the literature, and gives his judgment, based on thirty-two cases, which agrees with that of Boas and Kissmeyer.

CASE FOR DIAGNOSIS. E. G. GRAHAM LITTLE, Proc. Roy. Soc. Med. **13**: 13 (Dec.) 1919.

A school boy, aged 15, had a translucent waxy tumor on the inner surface of the right ala nasi, about one-fourth inch above the surface and one-half inch in diameter. It had recurred after attempted surgical removal, and radium treatment had not affected it. Diagnoses of rodent ulcer, milium (atypical) and sebaceous nevus were entertained.

GUY, Pittsburgh.

A METHOD OF TREATING TINEA. C. J. GLEASON **1**:219 (Feb. 14) 1920.

Gleason has used a thin layer of the chrysophanic acid ointment (30 grains to the ounce of lanolin), spread all over the dhobie or washerman's itch, and a little beyond the outer borders of the tinea. A roentgen-ray application is made (dose not definitely given), but measured according to the author's experience. After the treatment the ointment is wiped off the skin, and in 90 per cent of the cases treated in this way one application was sufficient to cure; in a few a second was given to make certain. Neither the ointment nor the roentgen ray alone gave such results.

GOODMAN, New York.

LES HEMATODERMITES D'ORIGINE SYPHILITIQUE INDIRECTE. (INDIRECT HEMATODERMATITIDES OF SYPHILITIC ORIGIN). DR. LEREDDE, Bull. Soc. franç. de dermat. et syph. **7**:282, 1919.

Leredde used antisyphilitic treatment in three cases, respectively, prurigo, acute eczema and an undiagnosed itching dermatitis. The father of the first patient had syphilis; in the second case both parents had syphilis; while in the third the patient gave a positive Wassermann reaction. Marked improvement in the skin condition followed antisyphilitic treatment, and Leredde suggests that many dermatoses are indirectly due to syphilitic infection.

SENEAR, Chicago.

A CASE OF HERPES ZOSTER. H. W. BARKER, Lancet **197**:1136 (Dec. 29) 1919.

The case reported is of unusual interest because two distinct areas on the same side of the body were involved: the ophthalmic division of the fifth nerve and the seventh intercostal nerve. The author was unable to find any record of zoster occurring simultaneously on the face and trunk.

WAUGH, Chicago.

A CASE OF MULTIPLE INFECTIVE LYMPHANGIO-ENDOTHELIOMATA. GEORGE PERNET, Proc. Roy. Soc. Med. **13**:17 (Dec.) 1919.

About eight years after the great toe had been amputated on account of a malignant growth, there appeared a number of small brownish, translucent appearing, cherry-stone-sized tumors over the shin of the same leg. The microscopic picture suggested endotheliomas to the pathologist. Dr. Adamson pronounced it the typical structure of carcinoma deposits in the lymphatics.

GUY, Pittsburgh.

SCLERODERMIE ET TRAUMATISME (SCLERODERMIA AND TRAUMATISM). R. BURNIER, Bull. Soc. franç. de dermat. et syph. **7**:294, 1919.

Burnier describes a case of scleroderma occurring at the site of a traumatism and limited to the injured area.

SENEAR, Chicago.

CASE FOR DIAGNOSIS. J. M. H. MACLEOD, Proc. Roy. Soc. Med. **13**: 22 (Dec.) 1919.

The patient had a large number of lesions on the legs, feet, arms, back and shoulders. For the most part they comprised depressed scars, the result of breaking down nodules. Glanders, dermatitis artefacta, sporotrichosis and scrofulous gumma were considered in diagnosis.

GUY, Pittsburgh.

UN CAS DE GRANULOME ANNULARE (A CASE OF GRANULOMA ANNULARE). MILAN, SAUPHER and THIBAUT, Bull. Soc. franç. de dermat. et syph. **7**:269, 1919.

The authors describe the clinical, physical and microscopic findings in a case of granuloma annulare. Findings strongly suggestive of tuberculosis were present.

SENEAR, Chicago.

CASE OF "ERYTHRODERMIE CONGENITALE ICHTHYOSIFORME." H. W. BARBER, Proc. Roy. Soc. Med. **13**:22 (Dec.) 1919.

The condition began at the age of 3, when the skin of the trunk and limbs gradually became roughened, in places reddened and covered with horny growths. In some places the skin was normal. A peculiar musty odor, such as Darier described in his case, was noted.

GUY, Pittsburgh.

TACHES ET TUMEURS PIGMENTEES DE LA PEAU CHEZ UN EPILEPTIQUE (MACULES AND PIGMENTED TUMORS OF THE SKIN IN AN EPILEPTIC). OLGA ELIASCHEFF, Bull. Soc. franç. dermat. et syph. No. 8, 324, 1919.

Eliascheff discusses a case in which the diagnosis rests between leprosy, xanthoma and Kaposi's sarcomatosis. Darier felt that the case was related to the latter disease but that it was a pigmentary, nonhemorrhagic form.

SENEAR, Chicago.

# Society Transactions

## NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

*Regular Meeting, May 4, 1920*

JOHN E. LANE, M.D., *Chairman*

HEMIATROPHIA FACIALIS. Presented by DR. WISE.

The patient was a little girl, aged 5, from Dr. Fordyce's clinic. The right side of her face was flattened. Two years previously she had been presented before the Section with a typical scleroderma, which was said to have followed the extraction of a right lower molar. She had been treated with pituitary and thyroid extract, and while the skin softened, the atrophy of the skin and superior maxillary bone on that side remained unaffected. There was no paralysis or sensory disturbance.

DISCUSSION

DR. LEVIN told of a similar case presented by him at a previous meeting of the Section in which there was also atrophy of the bone. In this case the patches of scleroderma had disappeared under the administration of thyroid.

VON RECKLINGHAUSEN'S DISEASE. Presented by DR. TRIMBLE.

A child, about 12 years of age, presented an unusually early development of the disease. When the case was first seen it was thought to be only a pigmentation, but closer examination revealed tumors which were not at all pronounced.

DISCUSSION

DR. POLLITZER said that in Recklinghausen's disease there was a triad of symptoms which this child presented—pigmentation, neurofibromas and mental deficiency. She was in a class in school in which her mates were 8 or 9. She was three or four years behind in her mental development.

TINEA UNGUIUM. Presented by DR. HOWARD FOX.

P. A., a colored man, 25 years of age, under charge of the U. S. Public Health Service, had a disease of the nails which was first noticed nineteen months previously while he was serving as a soldier in France. He was working in a machine shop at the time and could not give any suggestion as to the origin of the condition. The right middle finger first became diseased, and within a month nearly all the fingers and toe nails had become involved. Since that time the process had progressed slowly, extending from the free borders of the nails toward their roots. Examination disclosed that all the nails of the hands were affected, except the little finger of the right and thumb and little finger of the left hand. All the toe-nails were likewise involved except that of the middle left toe. The nails showed varying degrees

of dystrophy, affecting particularly the distal ends. One of the nails showed a slight chipping of the free border and a slight subungual hyperkeratosis—the patient stating that "all the nails began that way." There was an entire absence of paronychia, and no eruption was noted elsewhere. Three massive doses of roentgen ray given recently at monthly intervals had as yet caused no improvement. Several previous attempts to find the ringworm fungus had failed.

On the day after presentation a specimen which had remained for twenty-four hours in 40 per cent. sodium hydrate solution was examined and a mycelium and spores in great abundance were found. No growths had as yet appeared in a culture.

LUPUS VULGARIS. Presented by DR. GILMOUR.

The nose of F. L., a married woman, born in Italy, began to be red about eight years ago and progressed to the present condition. She was treated in the German Hospital about five years ago, and was under treatment there for about two years. She had had roentgen-ray treatment and also iodid injections, and about a year ago was treated with carbon dioxid in the DeMilt Dispensary.

INFECTIOUS ECZEMATOID DERMATITIS. Presented by DR. ABRAMOWITZ.

Edward D., aged 10, of Italian parentage, was from the service of Dr. Fordyce at the Vanderbilt Clinic. The mother of the child stated that the skin condition had existed for two years. The lesions began in a small area on the right calf after an attack of pneumonia. The lesions on the neck and trunk were arranged in a band-like form about 2 inches wide and consisted of a thickened, erythematous small, papular, scaly dermatitis. The entire circumference of the leg was covered by a weeping and also purulent exudate, from which it was difficult to remove the bandages. An exposed cutis with numerous pustules and erythematous dermatitis completed the picture in this area. A few isolated crusted papules were present on the trunk. The inguinal glands were enlarged to the size of a bird's egg. The axillary glands were slightly enlarged.

DISCUSSION

DR. POLLITZER said that the case impressed him as one of the most interesting of those presented. He wished to point out that the eczematous lesions presented a striking localization; they were limited to the extensor surfaces of the extremities, leaving the flexor surfaces entirely free—an unusual distribution for eczema. The case was one that could not be disposed of at a glance, but it seemed to him to be a prurigo eczematized by scratching.

DR. GILMOUR also inclined to the diagnosis of prurigo, and directed attention to the lesions in the groins. Had it been a virulent infection, some of these would doubtless have broken down. Such enlargements were common in prurigo.

DR. LEVIN said that against its being an infectious eczematoid dermatitis was the presence of most of the lesions on the extensor rather than on the flexor surfaces, and the absence of any pustules or pustular patches. It seemed to be a case of chronic pruritus with a secondary eczema. A blood count should be made to rule out a blood condition.

DR. BRENNER (by invitation) said that he had been impressed by the idea that it was primarily a condition of general malnutrition and that probably in the zeal of the dermatologists more attention had been paid to local treatment than to a general study of the systemic condition. Recently a series of papers had been published on the suboxidation syndrome, which referred especially to the constituents of the blood; and by the elimination of fats and sugars from the diet and the substitution of cottonseed oil, etc., it had been possible to regulate the internal secretions so as to overcome the skin conditions. While the local condition need not be neglected, it would seem that more attention should be given to the general condition, i. e., a searching of the blood for creatinin and sugar, and the ascertaining of whether the lesions were not due to some internal condition rather than to a parasite. The same would apply to a great many dermatologic cases, as not enough blood work is done to ascertain what is happening to the nourishment of the skin, especially in children.

DR. POLLITZER said he was in complete harmony with Dr. Brenner in not regarding all skin diseases as purely local processes. He thought Dr. Brenner was mistaken in attributing a contrary belief to dermatologists in general. While a large number of dermatoses were strictly disorders of the skin, there were a great many skin diseases in which the cutaneous disturbance was the result of an internal or systemic disease. This fact was so elementary that dermatologists did not think it necessary to refer to it in every case. The disease whose cutaneous manifestation we call prurigo is an excellent example of a skin disease produced as the result of a systemic disorder.

DR. BRENNER said that he had evidently been misunderstood, for he merely wished to emphasize the fact that one should remember that many skin diseases were due to systemic conditions and that one should guard against considering them purely local.

DR. LEVIN said they had studied the blood chemistry of about 200 patients with cutaneous conditions. As a result of his experience, he believed the blood chemistry of this patient would reveal nothing abnormal, except possibly a low carbon dioxid content.

DR. BECHET could not agree with the diagnosis of prurigo. He did not think that the presence of the enlarged glands necessarily indicated that the case was one of prurigo; they could be caused by septic absorption from an infectious eczema. The boy had a large scaly patch back of the ear which looked like a typical eczema. He was inclined to consider it a case of ordinary eczema with secondary infection and subsequent enlargement of the lymphatic glands.

DR. POLLITZER remarked that while a great deal had been said about the eczematous lesions no one had referred to a different class of lesions which was noted particularly on the back of the patient and especially over the shoulder blades. This region was dotted with small discrete scratched papules and felt like a nutmeg grater. This was not eczema and did not harmonize with the diagnosis of eczema in other regions. On the other hand, a badly scratched prurigo could simulate an eczema. Those who dwelt mainly on the eczematous lesions should remember that there were other lesions that were distinctly those of prurigo. The distribution of the eczematoid areas, the occurrence of distinct lesions of prurigo, and the enlarged lymph nodes indicated prurigo. Whether or not the whole condition was due to leukemia or to some endocrine or other disturbance, would require further study.

Dr. Abramowitz said that the patient had come to the clinic the day before presentation, so that no detailed study had been made. The eruption to which Dr. Pollitzer referred was much more noticeable in the daylight. Most attention was attracted by the band-like eruption on the neck, arms, and trunk and the pyodermia of the legs, which might account for the enlarged inguinal glands. It was thought possible that the dry eczematous lesions elsewhere on the body had probably at other times also taken on the pyodermatous nature, and hence it was considered an eczematoid dermatitis. It was difficult to form any conclusion at present. The prurigo-like papules on the body would be watched to see whether they would develop into an eczema or disappear. No history of an exciting suppurative process could be obtained.

BLASTOMYCOSIS. Presented by Dr. Binford Throne.

A horse driver had a lesion about 3 by 4 inches in size and situated on the anterior surface of the left wrist. It was granulomatous in character, slightly verrucous, with miliary abscesses. The onset of the disease occurred in June, 1918.

The section showed blastomycoses.

TYLOSIS PALMARIS HEREDITARIA. Presented by Dr. Binford Throne.

Mrs. E. T., born in Italy, and her three children, aged 13, 11 and 4, respectively, presented themselves at Dr. Whitehouse's service at the Skin and Cancer Hospital, April 21, 1920. All showed extensive tylosis palmaris and the oldest, in addition to the palmar condition, had involvement of the plantar surface of both feet. In all cases the disease began early in infancy. Mrs. T. said that her mother showed the same condition. No history of consanguinity could be obtained.

PITYRIASIS ROSEA IN A NEGRO. Presented by Dr. Howard Fox and Dr. B. F. Ochs.

G. T., a negro, aged 38, presented on the trunk a fairly profuse eruption of superficial inflammatory scaly lesions of the punctate, macular and circinate type. The general eruption was of two weeks' duration, and several days before its appearance an unusual patch, oval in shape and an inch in length had appeared on the upper portion of the right thigh. The patient, who was a large robust man, apparently in excellent health, was unable to suggest any cause for the appearance of the eruption.

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## NEW YORK DERMATOLOGICAL SOCIETY

*Regular Meeting, May 25, 1920*

George M. MacKee, M.D., *President*

NECROTIC GRANULOMA — TUBERCULOSIS? Presented by Dr. Winfield.

Miss H., aged 22, had been under observation since November, 1919. She was one of the bacteriologists of the Department of Health. In September, 1919, she was vaccinated; in a short time the vaccination became inflamed and

purulent, but it finally healed after about six weeks, forming a keloid scar. While the inflammation in the vaccination was beginning to subside, a pustule developed on the arm about 2 inches from the vaccination. At first, she paid no attention to it, but when it began to enlarge she consulted a physician on the laboratory staff, who referred her to Dr. Winfield.

At that time, the lesion was an indurated nodule with a necrotic center elevated about one-eighth inch above the skin. A tentative diagnosis of pyogenic granuloma was made and treatment for that condition was instituted. In about a month the necrotic center had cleared up and the elevation was considerably lowered, but since that time there had been little change, except that the induration had grown larger and deeper.

The case was presented for diagnosis—although the suspicion of tuberculous granuloma was entertained—and for suggestions as to treatment.

DISCUSSION

DR. FORDYCE inclined to the suggestion of tuberculous trouble.

DR. WILLIAMS thought it was a tuberculous lesion and that it should be excised. A definite diagnosis could then be made by microscopic examination of the specimen.

DR. HIGHMAN agreed with Dr. Williams that it was a tuberculous nodule and should be excised.

CASE FOR DIAGNOSIS. Presented by DR. LANE.

W. R. V-D., a man of 30, born in New Haven, a chauffeur, had lesions that were impossible to describe in detail as they were of so great variety, but it was hoped to make a detailed study of the patient later. He had been seen only once, a few days before. There was a generalized eruption on nearly the whole body, except the face and scalp. It started twelve years before as a general redness on the inner side of the right thigh, and had gradually progressed, developing symmetrically. It was most marked on the inner side of the thighs, the legs—front and back—the front of the arms and adjacent portions of the chest, and the back of the forearms. The most prominent characteristic was a marked telangiectasia, and in the centers of the larger patches, atrophy without induration. There were healed and unhealed ulcerations in the center of the patches on the right thigh and leg. On the areas where the lesions were new, there were small red spots at the sites of the hair follicles which at a distance gave the appearance of pityriasis rubra pilaris. There was no keratosis, the skin being perfectly free over these areas, but there were no hairs on them. A specimen of blood had been taken for a Wassermann test, but the report had not been received. The blood count was practically normal. Physical examination showed nothing except a soft systolic murmur at the second right interspace.

DISCUSSION

DR. WHITEHOUSE said he could throw no light on the case. There was no question of the angiomatous character of the lesions. It conformed to the type of angioma serpiginosum, but was associated with atrophy. It was altogether unlike anything he had seen. The ulcerations on the leg were peculiar.

DR. HIGHMAN said it was one of the most significant cases presented before the Society during the year. In some respects it suggested angioma

serpiginosum, but in other particulars it seemed like Majocchi's disease. It also reminded him of Stoke's case of specific telangiectasis. The association of distinct ulcerations made him wonder whether the entire group of capillary lesions of the skin might not be closely related to similar processes in the larger vessels supplying the tissues subjacent to the skin. That was an impression he had had for a long time, and it seemed to be corroborated in this group of cases. Raynaud's disease, and even Buerger's disease, might represent differences of degree and not of kind. This case opened up a new field of thought.

Dr. Howard Fox thought that the greater part of the eruption closely resembled angioma serpiginosum. He was unable to account for the ulceration.

Dr. Wise agreed with those speakers who thought that the case resembled angioma serpiginosum, but there were so many features of the eruption that differed from those of angioma serpiginosum that he did not believe that to be the correct diagnosis. He made the diagnosis of poikilodermia vascularis atrophicans (Jacobi) and exhibited the article and the cuts referring to that disease in the *Ikonographia Dermatologica.*

Dr. Winfield agreed with Dr. Wise and others who thought the case resembled angioma serpiginosum.

THROMBO-ANGEITIS OBLITERANS. Presented by Dr. Wise.

A man, referred by Dr. Mandelbaum, aged about 38, had had the condition for ten years. It began as a small ulceration between the fourth and fifth toes of the right foot, which was operated on and removed with some involved bone. The ulceration presented was of three years' duration and was located on the dorsum of the foot. The patient suffered intense pain at all times, and was presented for consultation in regard to the advisability of amputation and if so, the best site for it. The small toe had been amputated and a part of the metatarsal bone at the same time. Dr. Leo Buerger had paid quite a little attention to the patient at one time but it was not known what advice he gave the young man—whether to leave it alone or to have an amputation.

DISCUSSION

Dr. Winfield said that the higher the amputation was made the better.

Dr. Fordyce recalled a case of Buerger's disease in which the patient had lost one of his toes. The Wassermann reaction was negative, but in spite of the blood findings the man was put on antisyphilitic treatment. Later the Wassermann reaction became positive. This was the only case of the kind he had seen in which the Wassermann reaction was positive. The patient developed no trouble after persistent treatment.

Dr. Williams said that the man had been under his care at the Skin and Cancer Hospital, and had improved for a time under large doses of potassium iodid.

Dr. Highman spoke of recent reports from Japan to the effect that these cases clear up at the seashore with wet dressings of sea water and exposure to the general tonic of the seashore life. Whether such treatment would be of any value in this instance, he did not know.

TATTOOING. Presented by Dr. Howard Fox.

N. A., an Armenian girl, 14 years of age, three years before, during the war, had been captured by the Turks and forced to become an inmate of a Turkish harem. As a brand of ownership, various bluish marks had been tattooed on her forehead, nose, temporal regions and chin.

DISCUSSION

Dr. Pels (by invitation) said that he had had some results with the desiccation treatment, using a unipolar method. Under local anesthesia and employing a fine operating needle, the destroyed tissue was subsequently removed with a small curet, at least as much as possible. The wound was permitted to heal up under aseptic conditions. The entire pigmented area, however, could not be destroyed without leaving much scarring, but under these conditions the cosmetic result was fair, and there was a resultant smooth scar which had a more satisfactory effect than the tattooing.

APHTHOUS STOMATITIS OF TWENTY-THREE YEARS DURATION. Presented by Dr. Howard Fox.

M. R., a man, aged 36, born in the United States, had several brothers and sisters who had suffered at times from a condition similar to his but in a much milder form. As a child he had had measles, mumps and frequent attacks of sore throat and frost bite of his toes. Since adult age he had suffered from dry pleurisy several times. On one occasion he passed a large amount of mucus from the bowel, which was seen by a physician. In the spring of 1918 he was treated at the Johns Hopkins Hospital for two months, a diagnosis of mucous colitis and aphthous stomatitis being made. The present disease began at the age of 13 and had continued to the present time. He had had a half dozen attacks yearly, lasting from two weeks to two months. The longest period of freedom from lesions of the mouth was six months. According to his statement, the sores in the mouth appeared either singly or as many as a half dozen at one time. They began as "pimples," soon becoming open sores, which were more or less painful, especially at the beginning. At times they interfered with sleep and caused thickness of speech. His appetite was poor, his bowels were constipated and he often suffered from marked flatulence. The patient appeared to be in fair health. He was of medium height and weighed 130 pounds.

At the time of presentation, the lesions, with the exception of a small superficial ulceration on the mucous surface of the upper lip, had temporarily disappeared. When seen six weeks previously, he presented four ulcerations of the mouth, two on the mucous surface of the upper lip, one on the buccal mucous membrane, opposite the last molar and one on the anterior pillar of the fauces. The size and depth of the ulcers increased in the order above mentioned, that on the fauces being dime sized. They were all moderately deep with elevated, angry red looking borders and yellowish centers. They were quite tender to the touch.

The obstinacy of the case was shown by a letter from the patient's brother, a well known physician, who said that "he had consulted many physicians and had been the subject of innumerable examinations, bacteriologic and pathologic surveys, blood counts, etc. So far he had resisted all efforts, medical, physical, psychic, hygienic, climatic, etc." The Wassermann reaction had repeatedly been negative and there was no history of syphilitic infection. There had

been no improvement from either mercury or arsphenamin. Examination of the teeth showed no apical infection. The uric acid and sugar contents of the blood were normal; there was no evidence of acidosis on testing the alveolar air. A section of one of the ulcers had been histologically examined and the following report made by Dr. Pels: "There was a very cellular granulating tissue, some edema and fairly numerous collections of red blood cells; numerous infiltrating cells which consisted chiefly of small mononuclear leukocytes and a few polymorphonuclear cells. There were a fair number of newly formed blood vessels, and in some areas there appeared to be whorls of new connective tissue around the small blood vessels. There were also a few epithelioid cells."

As the examination of the stool had shown it to be "highly acid and extremely toxic," he was given a series of implantations of live colon bacilli, preceded by a series of alkaline enemas. While the patient was now nearly free of lesions, it was of course impossible as yet to say whether the improvement was due to the intestinal treatment, owing to the spontaneous disappearance of all of his previous attacks.

### DISCUSSION

Dr. Isaac R. Pels (by invitation) said that the case had been one of considerable interest. The patient was seen a little over two months before and then had a number of ulcers on his tongue a little to the left—one on the right tonsil, and a large one on the right upper lip. In appearance they were all practically the same as the largest one on the lip, which measured approximately 1.5 cm. in diameter. They were characterized by a redundant appearance of the granulation, were sharply defined, rounded with no undermining of the edges, and a grayish-white granulation tissue which had no tendency to bleed. Scrapings made from this ulcer showed in two specimens merely what was considered foreign material, probably cotton or gauze fibers, and no definite mycelium. More complete examination showed nothing definite. The tonsils were fibrosed and cryptic, the tongue slightly coated, the teeth in fair condition. All the glands under the lower jaw were palpable, and there was distinct evidence of Fordyce's disease, especially on the lips and pillars of the tonsils, as well as on the mucous membrane of the cheeks. The biopsy specimen showed nothing distinctive, merely a picture of granulation tissue with active proliferation of the fibrous tissue. Dr. Pels said that his impression was that the condition was probably due to some metabolism deficiency or to some condition similar to the mechanism of herpes zoster, or to a combination of the two. As the patient had been under observation for only a brief time, a complete medical survey had not been made. This, together with a special study from the standpoint of tuberculosis, would seem to be the line of investigation to be followed.

Dr. MacKee said that he had obtained cultures of both the streptococcus and staphylococcus in such cases; also, that he had tried autogenous vaccines without favorable result.

Dr. Fordyce said that several cases of this kind had come under his observation during the past ten years. He had been unable to find any description of the condition except in Sutton's "Diseases of the Skin," in which it was described under the name of periadenitis mucosa necrotica recurrens. In his experience, the lesions have begun as small papules which rapidly break down and leave a small excoriated ulcer. They occur on the tongue and on various parts of the oral mucosa; they heal in about ten days

or two weeks and almost invariably recur. He had one patient who had suffered from these lesions for many years; in addition to the mouth lesions, she had lesions on the vulva. This patient said that her mother and other members of the family had been similarly afflicted. The possible association of the condition with tuberculosis had suggested itself to him, and he had thought that the lesions on the mucous membranes were perhaps analogous to the papulonecrotic tuberculid seen on the skin. This, of course, was only a suggestion, as he had no direct evidence to support this theory.

MORPHEA GUTTATA. Presented by Dr. George H. Fox.

The patient, Mrs. S., exhibited an eruption, chiefly on the neck and waist and beneath the breasts. It began a year ago, near the vulva. The lesions were numerous and small, from pinpoint to split-pea size. Many showed a marked border and some showed a flat scaly surface. Some isolated papular lesions had a crusted center or one that was pitted, resembling lichen planus lesions, but there was a tendency of the lesions to coalesce and form linear or irregular ivory-like patches with the characteristic dry crinkled surface of morphea. There were no subjective symptoms and no family history, nor any apparent cause for the condition. During the past six weeks the patient's general condition had improved under diet and daily exercise.

DERMATITIS DYSMENORRHEICA. Presented by Dr. Wise.

A matron, aged 30, who had been referred by Dr. Katz, stated that she had had an eruption on the face and left breast with each menstrual period for the last two years. The eruption consisted of slightly edematous erythemato-vesicular patches which were somewhat painful. There was no evidence of its having been artificially produced. When the eruption disappeared it left a slight pigmentation, with a fading brownish hemorrhagic punctum in each follicle. Gynecologic examination revealed nothing but a tear in the cervix. She had been referred to Dr. Casamajor for consultation. He stated that the matter of psychoneurosis must be held under consideration, and that he did not believe the eruption to be self-inflicted.

DISCUSSION

Dr. Whitehouse said that in spite of the apparent phlegmatic temperament of the patient, he was inclined to consider the lesion a factitious one.

Dr. MacKee expressed the opinion that it was malingering, the result of hysteria associated with menstruation. The woman became hysterical at the time, and probably did not realize that she had injured the skin.

Dr. Howard Fox thought the eruption was self-inflicted, the lesions looking as though the patient had used sandpaper on her face.

Dr. Wise said that in five cases described by Matzenauer and Polland these authors demonstrated that it was not an artificial dermatitis, not self-inflicted. Dr. Casamajor had examined the woman and had been unable to elicit any history suggestive of an artificial dermatosis.

It seemed to be a spontaneously appearing condition appearing coincidentally with the menstrual period, identical with the eruptions described by Matzenauer and Polland.

Note: This case will be described in detail later.

A PECULIAR PAPULAR ERUPTION OF THE AXILLAE. Presented by Dr. Trimble.

A young woman, aged 29, born in Ireland, had in both axillae, especially on the anterior folds, great numbers of small papules about the color of the normal skin. These itched intensely. The duration of the trouble was three years, and it had slowly progressed from the beginning. The case was similar to the ones presented by Drs. Fox, Fordyce and others several years ago. The papules were about the size of the head of a small match and although situated close together, they were all discrete.

DISCUSSION

Dr. Fordyce said that since his observation of the original case described by Dr. Fox, he had seen a number of patients with this trouble. The sites of election are the axillae, the skin about the nipple and the suprapubic region. The lesions are noninflammatory and usually light red or yellowish in color; they itch intensely and are resistant to most of the ordinary antipruritics. Histologically, there is a marked hyperplasia of the epidermis, chiefly about the sweat duct orifices. The sweat coils below the epidermic lesions are greatly dilated. It is impossible to say whether the epithelial change is the result of an irritant from the sweat glands or whether the change in the sweat glands is due to a primary epithelial change.

Dr. Whitehouse agreed with one or two of the other gentlemen who observed that the axillary space was free from papular infiltrated lesions, and said it hardly seemed analogous to the cases reported under the title mentioned.

Dr. Highman remarked that the lesions in the case suggested the type described by Jadasohn as lichen trichophyticus, and he referred to Ormsby's paper and some European writers who spoke of aberrant forms of tinea, of which this case might be an example.

Dr. Howard Fox said that the eruption, which was not confined to the axillae, appeared to be an ordinary, thickened, intensely itchy patch of lichenification.

Dr. Lane thought the case was one of typical neurodermatitis with spots in a rather unusual location. The symmetry was also rather unusual. This diagnosis was still further borne out by the presence of a smaller typical patch of neurodermitis in the usual location on the nucha. He could see nothing to make Dr. Highman's suggestion of trichophytosis appear probable, although at present one did not dare to be positive on that disease before scrapings and cultures had been examined. The thickened skin, the exaggerated normal lines of the skin and the flat shiny papules were all characteristic of neurodermatitis and not of trichophytosis.

KELOID WITH GANGRENOUS CENTER. Presented by Dr. Trimble.

A woman, aged 32, born in the United States, had a keloid over the sternum which was operated on in October, 1919, by excision. The wound partially healed by granulation and was afterward skin grafted. The lesion returned, covering a large area, and showed a small keloid in each stitch hole. The interesting feature about the case was the small gangrenous adherent slough about the size of a hazelnut; it had not yet been ascertained to what this was due.

## MILIARY TUBERCULOSIS OF THE FACE. Presented by Dr. Trimble.

A mulatto woman, 23 years of age, born in the United States; had an eruption consisting of a number of round lesions—pinhead to match-head in size—scattered over the face and particularly on the vermilion border of both lips. The lesions were translucent, and some of them had a central depression or indentation. At the inner canthi of both eyes the lesions had coalesced, making a small group. The patient was also suffering from some eye trouble which had been diagnosed as metastatic choroiditis. The eruption on the face had lasted about one year. Biopsy showed the lesion to be a granuloma.

### DISCUSSION

Dr. Howard Fox said that the lesions on the nostrils were suggestive of lupus vulgaris. The eruption was similar to that of two cases (both patients were colored women) that he had recently presented, and he thought it certainly belonged to the class of disseminated lupus vulgaris.

Dr. MacKee said that this patient had been seen at the Vanderbilt Clinic about two years ago, and a microscopic examination then showed a typical tuberculous structure. At that time the condition yielded promptly to roentgen-ray treatment. The diagnosis was miliary tuberculosis.

## EPITHELIOMA LINGUAE. Presented by Dr. Wise.

A woman, aged 50, presented a lesion on the left side of the tongue, of three months' duration. It was an irregular ulcer, 1 cm. in diameter, with a rather dirty base. There were no palpable lymph nodes in the neck. A pathologic report had not yet been received. The patient was presented in order to obtain some suggestions as to the proper procedure in the case—whether to refer her to a hospital for immediate operation or to wait until further information had been secured as to the nature of the lesion.

### DISCUSSION

Dr. Fordyce suggested that the lesion might be tuberculosis of the tongue. He cited a case which resembled this one very much, in which the lesion was excised and found to be tuberculous.

Dr. Wise said the point referred to by Dr. Fordyce was the reason for presenting the case, for they had rather feared to make a biopsy. Would Dr. Fordyce approve of taking out a section?

Dr. Fordyce said that a wedge-shaped piece should be removed, taking out the whole of the lesion.

Dr. Highman said that in making a diagnosis of a lesion suspected of being epithelioma of the tongue, the excision should be made at a hospital, and while the patient is still narcotized a frozen section should be studied. If it proved to be epithelioma, the operation should proceed at once without waiting two or three days.

Dr. Fordyce said that the case should be treated just as are similar conditions in breast carcinoma, and if a frozen section were proper there it would be proper here. It is a routine procedure in all of the hospitals.

## PSORIASIS OF THE PALMS TREATED BY ROENTGEN RAY: QUESTION OF DOSAGE. Presented by Dr. Howard Fox.

H. M., a schoolboy, 11 years of age, had suffered from psoriasis on different parts of his body for nine years, and on the palms for the past five years. He was shown to aid in proving the presenter's opinion that the small doses of roentgen ray, ¼ Kolzknecht unit (skin distance), were not as effective as larger doses in treating psoriasis. The boy had been recently shown at the Manhattan Dermatological Society, at which time Dr. Wise stated that he had given the patient fourteen weekly treatments of ¼ Holzknect unit by roentgen ray. There was no perceptible improvement, and the case was considered to be roentgen-ray resistant. During the past ten weeks, Dr. Fox had given the patient 1 Holzknecht unit to one palm and ½ Holzknecht unit to the other, and concluded that the best results in this case were obtained from ½ Holzknecht unit given every two weeks. The large dose, given twice at monthly intervals, caused the lesion to clear up, but it relapsed partially. The half unit doses were given to both hands. As presented, both palms were practically smooth. He had previously been treated by chrysarobin, without benefit.

### DISCUSSION

Dr. Wise said that Dr. Fox had demonstrated his point in this case, but whether the same treatment would result so beneficially in other similar cases he greatly doubted.

Dr. MacKee agreed with Dr. Wise. In an extensive series of cases of psoriasis, when the lesions on one side of the body were treated fractionally and the lesions on the other side were treated intensively or semi-intensively, there was little difference in the results noted. On the whole, and for reasons that would require a long explanation, fractional treatment gave the best results and was the method of election. In these experiments, the total amount of ray administered in a month was the same with both methods. The speaker agreed with Dr Fox that one large dose (suberythema dose) would at times clear up psoriatic lesions that had failed to improve under the influence of fractional treatment, but this was not the usual phenomenon in his own experience. He was opposed to intensive treatment or to prolonged fractional treatment in a benign recurring disease, such as psoriasis, because in time the skin was likely to become dry from atrophy of the sweat and sebaceous glands, atrophic from changes in the connective tissue, and finally keratoses and other undesirable and even dangerous sequels might develop. If the lesions responded to a few fractional treatments and the patient remained free of eruption for a long period, such treatment was indicated; but if the eruption was or became recalcitrant, or new outbreaks were frequent, roentgenization in any form was contraindicated.

Dr. Whitehouse said he did not like to bring up a point that seemed like criticism, for he had great respect for the results of roentgen-ray treatment and what the speakers had done with it in certain distinct lines, but why should any case of psoriasis be treated with roentgen rays? He had never seen an eruption of psoriasis that could not be removed otherwise; and why should a generalized recurring eruption with a constitutional cause be treated with roentgen rays?

Dr. Howard Fox said that from his own experience he had for a long time felt that the larger doses had a better effect in psoriasis than the smaller ones.

He had expressed that opinion at a recent meeting at which the patient was shown, and the result had proved his contention in this particular case.

Dr. MacKee replied that one reason was that, as a rule—not always—the eruption would clear up more quickly than under any other therapy; another reason was that the patients preferred such treatment as they did not have to use disagreeable ointments. At the clinic, it was a rule that if the psoriatic lesions failed to clear up under three treatments of ¼ skin unit per week, some other method of treatment was instituted.

Dr. Whitehouse cited a case of symmetrical psoriasis that had been present on the forearms for seven years, which disappeared under one application of Vienna paste: salicylic acid, 20; chrysarobin, 20; oil of birch tar, 10; anhydrous wool fat, 25; soft soap, U. S. P., 25. The patient had a severe generalized dermatitis, but a second application was not necessary. The patches were sharply defined and infiltrated and had been present seven years.

Dr. G. H. Fox, referring to the test of using strong exposures on the lesions on one side and weak exposures on those of the other, said that it was impossible to cure half of the body of psoriasis. If you cure one side, the other side will soon get well spontaneously. A marked contrast of the two sides of the face can be produced by treating one side alone in acne, but this cannot be done in psoriasis.

Dr. Highman said that there were other points that might be brought up by Dr. Whitehouse's inquiry. As Dr. MacKee said, roentgen-ray treatment was cleaner, pleasanter and cheaper, and the patients preferred it. It was most convenient to the patient in regard to time, expense and pleasantness.

Dr. Howard Fox said he was speaking more particularly of psoriasis of the palms. The patient had previously been treated with chrysarobin by a well-known dermatologist.

Dr. Fordyce was opposed to the use of roentgen ray in treating generalized psoriasis unless the rays were employed by one thoroughly versed in modern technic. He had seen many cases of telangiectases following the use of the roentgen ray for this trouble.

Dr. MacKee said that Dr. Whitehouse's remarks were pertinent. The solution was not to carry roentgen-ray treatments too far. The skin would tolerate a certain amount of the rays (¼ skin unit per week for several weeks) without showing microscopic alteration. Even with slight changes, such as retardation of physiologic activity, there would be complete regeneration to the normal. It was safe, therefore, to administer a course of a few fractional treatments, and such courses might with safety be repeated occasionally over a number of years. No harm would be done so long as the dose was sufficiently small and the doses were not administered too close together.

Dr. Winfield asked whether it would not be better not to educate these patients to go to roentgenologists for treatment, since if they fell into the hands of men who were not dermatologists or roentgen-ray therapists, great harm might be done in the future, and the end results might be far more serious than the original disease.

Dr. MacKee said that in many instances a psoriatic eruption would disappear under the influence of the roentgen ray and the patient would remain free of eruption for months or even years—not by virtue of the roentgen ray, but for unknown reasons. Conversely, it was not infrequently observed that the patient developed immunity against the beneficial influence of the roentgen ray, which, in a way, is a protection for the patient. In such instances the roentgen ray should be discontinued.

It seemed to the speaker that the roentgen ray, if properly employed, was a good treatment for many cases of psoriasis, especially selected cases.

Dr. G. H. Fox said that a few years ago he made a diagnosis of dermatitis herpetiformis in the patient, but tonight he was reminded of cases seen by the hundreds fifty years ago in Hebra's clinic—cases of prurigo. The colorless nodules and the dry excoriated skin made it a perfect picture of what Hebra would have called prurigo.

Dr. Fordyce said that this case impressed him as one of prurigo. The lesions presented were very much like the typical prurigo papules.

Dr. Howard Fox said the eruption had been puzzling on account of its frequent changes in appearance, at one time resembling dermatitis herpetiformis, at another erythema multiforme, and at another prurigo. As yet he had not been able to influence the course of the eruption though many methods of treatment had been tried.

Dr. Williams inquired whether the child had been examined for local infections.

Dr. Fox replied that her teeth had been examined with the roentgen ray and no apical abscesses discovered. Her teeth had been put in good condition by a dentist. There was no source of infection in the tonsils. She had never suffered from attacks of sore throat.

Dr. Winfield said that while the case certainly looked like prurigo tonight, he had no doubt it was a case of dermatitis herpetiformis.

Dr. Highman asked how many times tonsils had been examined for focal infections when there were no dermatoses.

MELANOMA TREATED BY RADIUM. Presented by Dr. Clark.

Miss R., aged 35, born in the United States, as long as she could remember, had had a small, slightly raised dark mole on the outer surface of the upper part of the left forearm, about the size of a split pea. She had noticed no change in this lesion until about eighteen months ago, when, without apparent cause the lesion began to grow rapidly.

When first seen, six months before, the lesion was the size of a 50-cent piece, was distinctly raised, and the surface was warty with a scabbed condition over the central part. It would bleed whenever it was bumped or the scab disturbed. Neither the epitrochlear nor the axillary glands of that side showed any enlargement. After consultation with surgeons, it was advised that a massive dose application of radium be made to the lesion. Because of its size, it was necessary to divide the area in order that the applicator might cover all parts, and an extensive exposure was made in this manner. A marked reaction resulted, followed by a heavy rupial covering. At the end of about eight weeks, the crust came off, and it was then noticed that there were still signs of the black melanotic lesion over the center of the exposed area. Another massive dose application was made, not as prolonged as the first, which was followed by a superficial ulceration and crusting. This crust came off six or seven weeks ago, leaving a small raw area in the center with three black melanotic spots around its edges. Since that time these melanotic spots had diminished in size almost to the point of disappearing, but the central superficial ulcerating area had shown no signs of healing. It gives a hot and burning sensation and when left dry tends to become covered with a scab with a superficial crust. The patient showed no glandular enlargement.

PAPULONECROTIC TUBERCULID. Presented by DR. WISE for DR. FORDYCE.

Y. J., a schoolgirl, aged 13, an American, exhibited an eruption which had been present for six years—lupus erythematosus on the scalp and nose, and a papulonecrotic tuberculid of the face, hands and arms. The lupus erythematosus involved the entire nose and on the scalp was present in patches from 1 to 5 cm. in diameter. The typical redness, adherent scale and telangiectasia were present, and the scalp lesions exhibited considerable atrophy and alopecia. The cheeks and both sides of the hands were the site of a papulonecrotic tuberculid with many dusky red papules from 1 to 5 mm. in diameter, interspersed with the pitted scars of previous lesions. The forehead, too, showed a few scars of acnitis, and the fingers had the frost-bitten appearance seen in lupus erythematosus. The histologic examination of one of the papules proved it to be a papulonecrotic tuberculid.

ALOPECIA TOTALIS. Presented by DR. SCHWARTZ.

The patient was a boy of 11 who had suffered from the condition exhibited for two years.

PAPULONECROTIC TUBERCULID. Presented by DR. WISE for DR. FORDYCE.

F. F., a Russian girl, aged 11½, had lived in the United States for ten years. She presented a papulonecrotic tuberculid of five years' duration, occupying the face and the extensor surfaces of the arms. There were found the typical small violaceous papules, from 1 to 5 mm. in diameter, each having a minute greenish-white central necrotic point. The usual small pitted scars were intermingled with the papules.

PARAPSORIASIS LICHENOIDES. Presented by DR. WISE.

An expert mechanic, aged 35, born in Holland, had been referred to the speaker by Dr. Wallhauser of Newark. When first seen, he presented an extensive eruption involving the arms, legs, thighs and neck. The lesions, which were numerous, were dusky red papules from 3 to 10 mm. in diameter, with a faint scaling. The duration of the condition was two years, and none of the lesions had disappeared. He received ¼ unit of roentgen-ray treatment weekly, and after six or eight weeks of treatment the improvement was 60 to 70 per cent. The lesions were not now so distinct as when Dr. Wallhauser had showed the case before another society about two months ago. Some had disappeared completely, others had faded to faint brownish macules.

MYCOSIS FUNGOIDES. Presented by DR. WISE for DR. FORDYCE.

F. E., aged 34, had previously been presented at other meetings with the diagnosis of possible mycosis fungoides and a tentative diagnosis of parapsoriasis en plaques. The patient also had alopecia and the hair became gray in patches. Dr. Fordyce did not present the case with the idea that the three conditions were related. A biopsy had been made and examined by several pathologists, none of whom decided on the diagnosis of mycosis fungoides. Dr. Pollitzer had called the speaker's attention to Darier's opinion, saying that

diagnosis in an early case is impossible, and the clinical diagnosis—whether mycosis or parapsoriasis—was still undecided. The duration of the condition was eight years. The patient did not complain of much itching.

LICHEN PLANUS IN THE MOUTH. Presented by Dr. Wise for Dr. Fordyce.

A young man exhibited lesions of the buccal mucosa which extended along the interdental line. There was a fine lacework of milky color, but no individual papules could be discerned. Subjective symptoms were entirely lacking and for this reason no history of the duration could be obtained. Lichen planus was the tentative diagnosis, no biopsy having been made.

URTICARIA PIGMENTOSA (ADULT TYPE). Presented by Dr. Wise for Dr. Fordyce.

J. F., a native of the United States, aged 42, a teamster, had a brown macular eruption of fifteen years' duration. The trunk was especially involved, and the rest of the body as well, except the face, hands and feet. The macules ranged from 1 to 7 mm. in diameter and when briskly rubbed were transformed into temporary wheals. A biopsy had been made, but the laboratory report had not yet been received. The patient stated that the eruption had appeared immediately following a chancre fifteen years previously. The Wassermann reaction was ++++.

CHROMOPHYTOSIS FOLLICULARIS. Presented by Dr. Wise.

I. R., a negro, aged 22, from Dr. Fordyce's clinic, was presented to show a rather unusual type of chromophytosis. There were faintly scaling macules over the clavicles and numerous follicular and lichenoid lesions. A scraping showed the typical fungus of chromophytosis.

DERMATITIS HERPETIFORMIS. Presented by Dr. Howard Fox.

A. M., a girl, 9 years of age, born in the United States, had previously been presented before the Manhattan Dermatological Society on April 13, 1918. The case presented two special points of interest: first, the occurrence of the eruption ten days after vaccination for smallpox, and second, the changing type of the eruption from time to time. The disease had existed for five years and with the exception of a remission for two months last summer, she had never been free from lesions. At present the eruption was mostly confined to the extensor surfaces of the forearms and presented shotty papules with an intense pruritus that closely simulated prurigo. On some previous occasions a picture of erythema multiforme with typical iris lesions was presented that would have been classic except for the presence of some excoriations. On other occasions during the past three years she had shown a typical eruption on the face, trunk and extremities of the papular type of dermatitis herpetiformis.

Efforts to ascertain the cause of the eruption had been unavailing. A physical examination by Dr. Longcope revealed nothing abnormal, except the eruption. Blood examinations were negative. Roentgen-ray examination of the tonsils and teeth revealed no evidence of focal infection. Cutaneous tests with twenty-six proteins were negative to all except coco and cornstarch. Salves containing the latter substance were accordingly omitted, but no

change in the patient's condition resulted. Examination of the stools showed them to be highly acid and extremely toxic with absence of colon bacilli. She was therefore given treatment by implantations of live colon bacillus, preceded by a series of alkaline enemas but there has been no improvement up to the present time.

PSORIASIS IN A DIABETIC ON STARVATION DIET. Presented by DR. HOWARD FOX.

J. K., an ex-soldier, 22 years of age, born in the United States, was shown through the courtesy of the U. S. Public Health Service. He had suffered from diabetes mellitus for the past six months, and at the time of presentation the urine contained 3 per cent. of glucose; he had lost 50 pounds since the beginning of his illness. He had been given the Allen (starvation) treatment. Five weeks before he presented a profuse eruption of typical guttate and nummular psoriasis of the scalp, trunk and extremities and a slight eruption on the face. The eruption was the first of the kind from which he had ever suffered.

SPOON NAILS (KOILONYCHIA). Presented by DR. HOWARD FOX.

J. W. C., a man, 26 years of age, born in the United States, a clerk, had a negative family history, none of his relatives having suffered from disease of the nails. As a child he had had scarlatina, diphtheria and measles. He was married seven years before presentation and had two apparently healthy children. Five years ago, subsequent to the birth of his children, he contracted syphilis and was treated by a well-known dermatologist. The Wassermann reaction at present is negative. He had at one time been a heavy whisky drinker. He was of nervous temperament and bit his nails frequently. The affection of the nails first appeared a little over a year ago, symmetrically affecting the thumb, index and middle finger nails of both hands. Examination showed a spoonlike hollowing of the distal two thirds to three fourths of these nails. The free ends were tilted upward, were brittle and showed a slight ungual hyperkeratosis. There was a lessening of the normal luster of the nails, the color not being markedly changed. There was no evidence of paronychia. The toe nails were not affected.

DIFFUSE SCLERODERMA. Presented by DR. HOWARD FOX.

S. N., a man, 22 years of age, born in the United States, a machinist, with a family history that was not significant, had suffered from scarlatina and measles in childhood. He had at one time been a great cigaret smoker. He denied venereal disease and did not drink alcohol. He had had a severe attack of pneumonia in the fall of 1918, from which he had made a slow convalescence. Previous to this attack his general health had always been good. The present illness began about two months after the attack of pneumonia, the patient first complaining of severe sharp pains in the knees when walking. This continued for about a month. He also suffered from attacks of vomiting which had continued every day up to the time of presentation. The attacks were severe at first, occurring after every meal and frequently between meals. At present they occurred only in the evening. He had lost 35 pounds since the beginning of his illness. He gave no history of cough or other symptoms suggesting tuberculosis.

He was poorly nourished, 5 feet 8½ inches in height, and weighed 114 pounds. There was a general firm, hard symmetrical, hidebound condition of the face, trunk and extremities. This was most marked in the hands which were cold and bluish. They showed a few small areas of vitiligo, some of them on previous sites of warty lesions removed by acid. There was no evidence of an associated Raynaud's disease. There was partial ankylosis of the joints of the fingers and wrist. The fingers, though stiff and hidebound, did not show pronounced tapering of the ends. The involvement of the cheeks made the face expressionless. The hair was dry, thick, brown and curly. The nails were normal. There was a good deal of dirty, yellowish-brown pigmentation, particularly on the trunk. There was a band of pigmentation about an inch wide along the lower dorsal and lumbar region of the spinal column. There were also larger areas of pigmentation over the scapulae, shoulders, backs of the arms and buttocks and to a less extent on the thighs. In places there was a slight scaling as seen in ichthyosis. There was no change in sensation to touch, pain or temperature or muscular sense. The reflexes were not pathologic.

Examination of the eyegrounds showed "marked dilatation of retinal arteries of the same caliber as the accompanying veins." The mouth, throat and organs of the chest and abdomen were apparently normal. The Wassermann reaction was negative. The urine showed a few granular casts but was otherwise normal. The blood pressure was 100 systolic, 80 diastolic. Blood examination showed: red cells, 5,600,000; hemoglobin, 95 per cent.; white cells, 9,200. Differential count: polymorphonuclears, 70 per cent.; lymphocytes, 22 per cent.; large mononuclears, 4 per cent.; eosinophils, 4 per cent. Blood chemistry: urea nitrogen, 11.5 per cent.; creatinin, 2 per cent.; uric acid, 3.1 per cent.; sugar, 110 mg. Coagulation time was six minutes. Roentgen-ray examination of the sella turcica showed "small clinoidals nearly in apposition." The patient was being treated with thyroid extract.

SARCOID. Presented by DR. KINGSBURY.

A young woman with lesions on the cheek, suggesting erythema multiforme or a toxemia due to pregnancy, gave a history of having had a similar condition when pregnant four years previously. When presented, she was in the fourth month of pregnancy, and the lesions had been present for two months.

HYDROA VACCINOFORME. Presented by DR. KINGSBURY.

A girl, aged 9, gave a history of having had the eruption last year and again this year. On exposure to the sun one week before, the eruption had appeared on the legs and arms.

EPITHELIOMA OF THE FINGER. Presented by DR. KINGSBURY.

A man, who had suffered from psoriasis for fifteen years, had an ulceration on the finger that had been present for over a year. There were keratoses on the backs of both hands, and this ulcer began on one of them. The patient also had an ulceration between his toes.

LICHEN PLANUS. Presented by DR. KINGSBURY.

The patient presented papular lesions on the thigh and a linear dispersion of lesions on the chest.

# Book Reviews

AN ATLAS OF THE PRIMARY AND CUTANEOUS LESIONS OF ACQUIRED SYPHILIS IN THE MALE. CHARLES F. WHITE and W. HERBERT BROWN. London: John Bale Sons, 1920.

The authors had an opportunity to make photographs of selected patients from 19,000 cases of syphilis that came under their observation. One purpose in presenting a selection of their collection in the form of an atlas was to aid in the early clinical diagnosis of initial lesions.

The majority of the photographs are stereoscopic, and the three dimension illusion when viewed through the instrument makes a better visual impression than the flat presentation.

Short notes and descriptions of the lesions are given. The text is based on the experiences of the authors. Although they admit that any classification of syphilitic chancres is difficult because types merge one into the other, they give this list with percentages based on an analysis of over 9,000 primary sores.

| Class of Sore | Per Cent. |
|---|---|
| Primary hunterian chancre | 13.45 |
| Primary granulating syphilitic sore: | |
| (*a*) Circular or oval | 21.21 |
| (*b*) Linear | 0.26 |
| Primary abrasive syphilitic sore | 2.96 |
| Primary papular syphilitic sore | 0.79 |
| Primary papulo-abrasive syphilitic sore | 29.31 |
| Primary ulcerative syphilitic sore | 2.28 |
| Primary phagedenic syphilitic sore | 0.79 |
| Primary meatal syphilitic sore | 2.50 |
| Primary intra-urethral syphilitic sore | 0.08 |
| Primary concealed syphilitic sore | 26.37 |

Only 131 cases of extragenital chancre were encountered in over 19,000 cases, and twelve stereoscopic pictures are given of the various types and locations.

To aid in the clinical differentiation, a description and photographs of nonsyphilitic or soft sores is given. One out of four lesions were of this character. The practitioner is warned to be certain of his diagnosis before telling the patient that he suffers from soft sores only, as he may have a double infection, or the syphilitic infection may make itself evident at the site of the soft sore or elsewhere. The use of the dark field illumination method for the demonstration of the syphilitic organism is urged.

Following the section on cutaneous syphilis is a short presentation of skin lesions which not infrequently are mistaken for syphilis.

Four colored plates are included, which are good examples of this type of work.

The atlas is valuable and should appeal especially to those who have not had the opportunity of seeing many clinical cases of dermatologic manifestations of syphilis.

SYPHILIS IN CHILDHOOD. LEONARD FINDLAY, M.D., D.Sc., F.R.F.P.S.G. London, Oxford Medical Publications, 1919. Pp. 150.

This is a clear, well written and exceptionally well printed book on syphilis in childhood, based almost exclusively on the studies of the author (some

in collaboration) at the Children's Hospital of Glasgow and at the Medical School of Glasgow University.

Findlay believes that of the terms "congenital syphilis" or "hereditary syphilis" the former is decidedly the better. An organismal disease cannot in the true sense of the term be hereditary. "Hereditary" implies some peculiarity or characteristic inherent in the germ cells, and appearing in one generation after another. Syphilis does not conform to this law.

Numerous histories of maternal and paternal syphilis are given in the discussion, and indeed, these case histories to the number of forty-seven are well distributed throughout the twelve chapters. The presentation of a chapter on "Acquired Syphilis in Childhood" should stimulate consideration of this phase of the subject.

There are six colored plates, thirty-seven other illustrations in the text, and four charts.

The book is worthy of interest not only to the practitioner, but also to the syphilologist and pediatrician.

RECENT ADVANCES IN THE TREATMENT OF SYPHILIS. By RAJENDRA KUMAR SEN, in charge of the Hospital and Dispensary of Dejoo Tea Co., Ltd. Cloth. Price, 3 Rs. Pp. 82. Calcutta: Butterworth & Co., 1919.

Sen presents the Prize Essay of the *Indian Medical Gazette* for the best paper on this subject. He gives an outline of the contributions toward the present knowledge of syphilis, quoting freely from the published articles of others. He includes his "Notes on Salvarsan" reprinted from the *Indian Medical Gazette* of August, 1914. Sen gives arsphenamin at intervals of four weeks, as he asserts that the drug given in doses of 6 dg. is not completely excreted even after three weeks.

The monograph gives no indication of the prevalence of syphilis in India. It is of no value to the syphilologist of this country.

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